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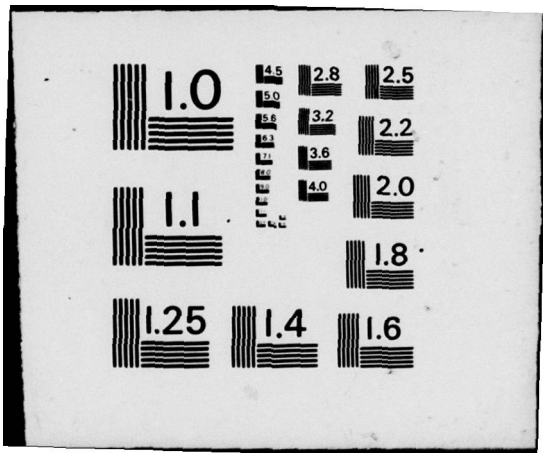
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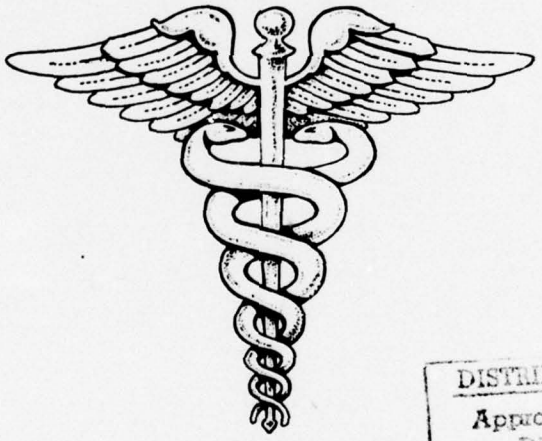
CLINICAL INVESTIGATION SERVICE

Annual Research Progress Report FY 1976



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FOREWORD

The Clinical Investigation Program at LAMC is guided by AR 40-38 and LAMC Regulation 70-10. The Clinical Investigation Service aids and advises investigators and coordinates efforts with LAIR. The Clinical Investigation and Human Use Committees meet monthly to review all proposals.

Proposals, preliminary findings, publications, and manpower are listed in this report.

MICHAEL M. BRONSHVAG
LTC, MC
Chief, Clinical Investigation Service

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Leith, JT; Lewinsky, BS; Smith P; Wishko, D: Effect of Bleomycin on Skin Reactions in Mice after Fractionated X-Irradiation. Submitted for Publication.

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Ring, G; Krames, E; Wallis, KL; Levinson, G; Shnider, SM: The Effect of Nitroprusside and Hydralazine on Uterine Blood Flow and Fetal Well - Being in the Hypertensive Pregnant Ewe. Submitted for publication.

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UNIT SUMMARY SHEET

Clinical Investigation Service, LAMC

There were 41 work unit in progress at the beginning of FY-76. During the year 11 were terminated, 11 were completed, 6 pending and 19 studies initiated. There are 44 ongoing projects at the closed of FY 76.

OBJECTIVES: To promote and coordinate clinical research within LAMC and exercise overall management response for clinical research activities to include planning, coordination, staff supervision, execution and review of all authorized clinical investigation projects which entail funding and/or other support by the Clinical Investigation Service. To coordinate with LAIR appropriate research efforts requiring technical support, to include experimental design, biostatistical analysis, consultation service and laboratory animal support. To provide editorial assistance to individual submitting manuscripts to In-house, regional and national journals.

TECHNICAL APPROACH: Research efforts of Letterman Army Medical Center staff are guided by Chief, Clinical Investigation Service through review of proposals and progress reports. The Clinical Investigation and Human Use Committees serve an educational as well as regulatory function in this regard. Monthly review of expenditures and regular inquiry into administrative matters keeps fiscal policy sound. The Deputy Commander is regularly apprised of progress and problems. Chief, Clinical Investigation Service regularly attends Letterman Army Institute of Research staff meetings to provide continued good communication between Letterman Army Medical Center, Chief, Clinical Investigation Service and Letterman Army Institute of Research.

Manpower: Current and authorized strength is outlined.

Description	Grade	MOS	Br	Auth	Actual	Name
C, Cl Invest Svc	05		MC	1	1	Bronshvag
Tech Pub Ed Med	09	01083	GS	1	1	Applewhite
Bio Lab Tech	07	00404	GS	1	1	Haug
Med Technologist	07	00644	GS	1	1	Polakoff
Med Technologist	07	00644	GS	1	1	Turner
Secy-Steno	05	00318	GS	1	1	Banks
Editorial Asst	05	01087	GS	1	1	Swee

Funding:	FY-76 PROGRAM
Civilian:	$71,254.28
Travel:	178.69
Support Agreement LAIR	$66,389.41
Supplies:	$20,000.00
Equipment:	$29,187.00

WORK UNIT NO. 109

TITLE OF PROJECT: LAMC DIG - Compliance Study

INVESTIGATORS: Principal: Carl C. Peck, LTC, MC

Associate: Thomas J. Egan, LTC, MC

OBJECTIVES: To compare serum digoxin concentrations(SDL) and stated digoxin intake histories obtained from an unannounced survey (Phase I) with SDL's obtained under conditions of known digoxin intake (Phase II) in a group of outpatients. From these comparisons, measures of compliance will be calculated. Some patient characteristics will then be correlated with compliance.

TECHNICAL APPROACH: Project terminated. Results reported in: Peck, CC: Compliance with Self-medication among outpatients, Present Concepts in Internal Medicine, 71-84, 1976; Peck,CC: Chapter 23 "Qualitative Aspects of Therapeutic Decision - Making" in Basic Principles of Clinical Pharmacology, KL Melmon and HF Morelli(Eds), 1976 (in press).

WORK UNIT NO. 110

TITLE OF PROJECT: Petrin(R)- C0743 Oral Pentri Nitrol Antianginal Agent Evaluation Phases I, II, and III.

INVESTIGATORS: Principal: Henry F. Bellaci, MAJ, MC

Associates: Gabriel Gregoratos, COL, MC
Larry L. Lawrence, LTC, MC
William C. Foote, MAJ, MC

OBJECTIVE: To evaluate pentrinitrol - C0743 as an efficacious antianginal agent by serial evaluation of exercise tolerance with treadmill stress testing. Patients were titrated to maximum Tolerated Dose to Determine any adverse reactions at high doses.

TECHNICAL APPROACH: This will be a double-blind placebo-controlled, single crossover trial of W2197 in anginal patients with two eight week treatment periods. The double-blind study is preceded by a single-blind phase. A period during which placebo is administered is followed by a period of varied dose administration to evaluate the individual patient's dose requirement prior to commencing the double-blind study. Also, a placebo period separates the dose individualization section of the study from the double-blind crossover portion of the study in order to re-establish baseline information. 20-25 patients with advanced ischemic heart disease(IHD) with anginal syndrome, functional capacity Class II-IV, according to the nomenclature for diagnosis of the heart of the American Heart Association shall be utilized. Their ages shall range from 40-75 years of age. In addition to the classical clinical history, the diagnosis of "angina" will be confirmed by: (a) positive exercise tolerance tesst terminated by pain and/or ischemic ECG changes, or coronary arteriography.

PROGRESS & RESULTS: 11 patients have been studied. Two patients were dropped due to insufficient symptoms for clinical evaluation. One patient dropped because he left the area. One patient expired while in Phase I (the placebo phase) - this patient had a prior myocardial infarction, hypertension and diabetes(insulin dependent). He was being maintained on appropriate needs for these conditions. A full report has been filed with the FDA. This patient's death was not considered to be related to this project by the FDA. Seven patients completed the study or were carried through 30 June 1976 with no adverse findings. Adverse reactions to high doses were restricted to headache and occasional dizziness. These effects dissipated either with reduction of dosage or after continued use of the drug.

FACILITIES TO BE USED: Letterman Army Medical Center and Warner-Lambert Research Institute.

FUND: Funded by Warner-Lambert REsearch Institute.

PUBLICATION & CONCLUSIONS: Since the evaluation of this drug is double-blind no conclusions can be drawn at this point until the code is broken and the results made known to us by Warner-Lambert.

WORK UNIT NO. 114

TITLE OF PROJECT: Clinical Trial of Hyperimmune Gamma Globulin for Prophylasix of Patients Receiving Multiple Blood Transfusions

INVESTIGATORS: Principal: Eugene P. Flannery, LTC, MC

Associate: Ms. Josephine Polakoff, GS7

OBJECTIVE: To determine if human serum gamma globulin with a significant HBab Titer protects against transfusion hepatitis; determine effective HBab liter, and determine if blood that contains HBAg by radioimmune assays but not by IEOP is infective.

TECHNICAL APPROACH: Project completed.

PROGRESS & RESULTS: The infrequent occurrence of hepatitis B in the transfused cardiac surgery patients in this study made it impossible to evaluate the efficacy of prophylactic gamma globulin administration in the prevention of posttransfusion hepatitis B. Only 2 of 20 probable cases(10%) and 3 of 43 probable plus questionable cases (7%) could be classified as related to hepatitis B infection based on both HB_sAg and anti-HB_s testing of serial serum specimens. Of the 2 probable hepatitis B infections, one patient received placebo and the other was inoculated with normal gamma globulin. The third questionable hepatitis B patient was in the placebo group. None of the three patients had anti-HB_s in his preoperative serum specimen and only one received a transfusion shown to contain HB_sAg by radioimmunoassay. One placebo-treated hepatitis B patient was icteric while the remaining two patients were anicteric. 15 patients in this study received blood that was negative for HB_sAg by CEP but was subsequently found after transfusion to be positive by RIA. 13 other patients who received only HB_sAg negative transfusion (by CEP and RIA) developed a B serological response without enzyme elevations.

CONCLUSIONS & PUBLICATION: Manuscript submitted to New England Journal of Medicine. Abstract was presented at the American Society of Hematology-Dallas, Texas, 8 Dec 75.

FUND: Funded by WRAMC.

WORK UNIT NO. 118

TITLE OF PROJECT: Levels of Gamma-Aminobutyric Acid in Brain during Monomethylhydrazine Intoxication and Vitamin B_6 Therapy

INVESTIGATORS: Principal: Robert W. Parzynski, GS7

Associate: Michael M. Bronshvag, LTC, MC

OBJECTIVE: To study what effect pyridoxine and pyridoxal forms of B_6 have on seizure activity and levels of GABA in brain of mice injected with MMH.

TECHNICAL APPROACH: Project completed. Manuscript prepared for publication. During the past year a technique for extraction and measurement of GABA was perfected and utilized to test over 200 mouse brains. Results of the testing indicated that convulsions in mice begin when GABA levels start to fall and do not occur, nor do GABA levels fall, when either pyridoxine or pyridoxal is administered concurrently. The biological significance of this is discussed.

FUND: None.

WORK UNIT NO. 120

TITLE OF PROJECT: Detection of Experimentally Induced Intravascular (Superior Sagittal Sinus) Thrombosis in Dogs and Sheep Using Radionuclide-Tagged Fibrinogen (131_I 123_I and 99mTc) and the Pho Gamma III Camera

INVESTIGATORS: Principal: Michael M. Bronshvag, LTC, MC

Associate: Daniel Haug, GS7

OBJECTIVE: To develop a method for detection of thrombosis and dorsal longitudinal sinus using high gamma emitter such as I_{123} and 99mTc complexed to clottable fibrinogen. Thereby, the gamma scanning camera could image such clots. If successful, this method may permit definitive diagnosis in diseases involving vessel occlusion without obvious infarction, such as superior sagittal sinus occlusion, asymptomatic carotid occlusion, and high grade obstruction or occlusion of individual coronary arteries. Therefore, this method might provide a relatively riskless way of selecting patients for invasive studies such as angiography, in hopes of detecting and correcting vascular obstruction or thrombosis before irreparable tissue infarction supervenes.

TECHNICAL APPROACH: Sheep will be anesthetized, and, using a midline incision, the frontal bone will be exposed. The sheep will be examined pre and post operatively by medical and veterinary clinicians. The radioactively tagged fibrinogen will be injected intravenously either before or after surgery, and imaging will be performed daily with LAIR's gamma camera. All animals will be sacrificed and autopsied. The dorsal longitudinal sinus and dura will be examined grossly and microscopically for operative trauma and presence and age of clot. The brains will be preserved in formalin and then serially sectioned, especially looking for spread of clot into cortical veins and also areas of hemorrhagic infarction (a frequent complication of clinical dural venous thrombosis)[15].

PROGRESS & RESULTS: Surgical procedures for inducing a dorsal longitudinal sinus occlusion in the dogs and the sheep have been successfully accomplished, using thin stainless steel or copper wire and the technique of incremental electrothrombosis. Successful occlusion of the sinus, without extension of clotting into cerebral brain, tissue infarction, or actual "cooking" of surrounding tissues is reliably identified by the presence of transient (but not persistent) high voltage slowing in the parasagittal area on the EEG. Over 50 attempts have been made to tag I^{123} and I^{131} to freshly separate fibrinogen. The iodine monochloride method, however at present reliable tagging (over 50% tagging of 50% clottable fibrinogen) occurs only 25% to 33% of the time. Satisfactory images have been obtained in two sheep using the gamma scanning camera. Further plans include continued attempts to reliably tag fibrinogen with I^{123}, in hopes of involving a method reliable enough to be clinical useful.

FACILITIES TO BE USED: Clinical Investigation Service's Laboratory LAIR.

FUND: $380.17.

PUBLICATION & CONCLUSIONS: None

WORK UNIT NO. 124

TITLE OF PROJECT: Normal Nerve Conduction in the First Year of Life

INVESTIGATORS: Principal: Francis B. Buda, MAJ, MC

Associate: Albert C. Molnar

OBJECTIVE: To determine comparable values for nerve conductions, motor and probably sensory in the first year of life.

TECHNICAL APPROACH: Project terminated due to transfer of co-worker.

WORK UNIT NO. 125

TITLE OF PROJECT: J5 Antiendotoxin Antiserum Study

INVESTIGATORS: Principal: Fred R. Stark, LTC, MC

Associate: Dr. Abraham I. Braude
Dr. E. J. Ziegler

OBJECTIVE: To test the ability of human antiserum against endotoxin to protect patients from death due to gram negative bacteremia.

TECHNICAL APPROACH: This study is a double blind trial of antiendotoxin antiserum prepared in human volunteers. The trial is conducted among high risk patients in early sepsis with presumed gram negative bacterial infections of the blood. The material for use has been tested individually for activity in protecting animals (mice) against endotoxin or sepsis challenge, as well as for sterility and pyrogenicity. Each volunteer patient receives 100-250 cc of antiserum during an early phase of presumed sepsis. Observations for untoward reactions, survival and complications are carefully recorded.

PROGRESS & RESULTS: A total of 20 patients have been entered in the trials at LAMC. The usual patient is an individual suffering from cancer with severe neutropenia. The overall short term mortality was less than 20%, lower than the published average for septic patients in this very high risk category. The referees have not yet broken the code in the trials, which include data from the University of California San Diego hospitals, the San Diego Naval Hospital, and Walter Reed General Hospital. A total of about 100 patients have been treated. No untoward reactions ascribable to the antiserum have been noted.

FACILITIES TO BE USED: Patients will be evaluated and treated at LAMC. Laboratory facilities for storage and processing of specimens will be at LAMC. Preparation and supply of experimental drugs will be accomplished by the University of California San Diego.

FUND: None

PUBLICATION & CONCLUSIONS: The success of this study has vital implications to military medicine. If antiendotoxin antibody raised against cell-wall defective coliform mutants is broadly protective against endotoxin, as has been shown in animals, vaccine trials in troops imminently exposed to trauma might have a profound impact on survival, as sepsis and endotoxemia appear to play a role in death from shock, in man and in many animal studies.
References: Endotoxin Symposium, Journal of Infectious Diseases, Suppl. August 1973.

WORK UNIT NO. 126

TITLE OF PROJECT: Electrophysiological Indicators of Infantile Deafness or Central Nervous System Maldevelopment or Malfunction

INVESTIGATORS: Principal: Francis B. Buda, MAJ, MC

Associates: None.

OBJECTIVE: An attempt to trace the normal evolution of the early auditory evoked response(AER) components (under 10 milliseconds) during the first two years of development in the normal child.

TECHNICAL APPROACH: 70 young children 1 day to 24 months of age will be selected for this study. Ages: newborns(40 wk gestation); 6 wks, 3 mons, 6 mos, 12 mos, 18 mos and 24 mos. After obtaining informed parental consent, the individual auditory evoked response(AER) determinations can be completed in approximately 15 minutes.

PROGRESS & RESULTS: Thus far the research investigation of the Auditory Evoked Response(AER) has led to the definition of the AER in different age groups. Specifically, in a paper presented to the Western EEG Society Meeting in February 1975 in Seattle, Washington, and in a paper published in Brain Research, volume 96, pages 361-366, 1975 the latencies of the wave forms in the AER were defined according to age from birth to adulthood. Work is continuing in order to identify infants and young children who have auditory difficulty before this difficulty is clinically apparent so as to initiate corrective measures at an early time. In addition, further definition of the use of the AER in acquired conditions in which there is brain stem malfunction is being investigated.

FACILITIES TO BE USED: Neurology Clinic LAMC

FUND:

PUBLICATION & CONCLUSIONS: Paper presented to the Western EEG Society Meeting in February 1975 in Seattle, Washington, and in a paper published in Brain Research, volume 96, pages 361-366, 1975.

WORK UNIT NO. 127

TITLE OF PROJECT: Rejection of Verrucae Vulgaris - A Clinical Therapeutic Trial I and II

INVESTIGATORS: Principal: Joseph H. Greenberg, MAJ, MC

Associate: Richard Odom, LTC, MC

OBJECTIVE: To determine if induction of a delayed hypersensitivity reaction over a verruca vulgaris will cause destruction of the verruca and possibly cause regression of other verrucae vulgaris not treated.

TECHNICAL APPROACH: Project is completed. 63 patients have been treated. Certain modalities seem to be efficacious. Ppd rhus and trichophyton had a response rate of 50-60%. The group of patients tested were mostly refractory to other therapies and therefore this may indicate successful therapy.

PUBLICATION & CONCLUSIONS: Immune therapy is another modality that can be used in wart therapy. It seems to be effective at times when other treatment modalities are not. This work was presented at the Tri-Services Dermatology Conference which was held at LAMC in April 1976.

WORK UNIT NO. 128

TITLE OF PROJECT: Polybrene Neutralization Determinations of Blood Heparin Levels Compared to other Lab Parameters of Heparin Activity in Common Clinical Usage

INVESTIGATORS: Principal: William Stone, MAJ, MC

Associate:

OBJECTIVE: To correlate plasma levels of heparin as measured with polybrene neutralization with tests of clinical clotting such as APTT, PTT, Lee White.

TECHNICAL APPROACH: Each patient, prior to being placed on heparin therapy will have the following baseline studies performed by the clinical research laboratory. (1) APTT 8cc; (2) Lee-White Clotting time (LWCT) 3 cc; Activated clotting time(ACT) 2cc; Polybrene neutralization 10cc. An IV infusion of heparin will be given in a dose determine by the primary physician. The studies enumerated in (1) will be repeated at 30', 1 hour., and every hour thereafter until a second dose of heparin is given up to six hours. Decay curves of heparin activity using APTT, LWCT, ACT, and polybrene neutralization can be plotted from the data obtained. Comparison can be made between polybrene neutralization and the more commonly accepted modes of monitoring heparin activity, i.e., LWCT and ACT, to determine its clinical usefulness.

PROGRESS & RESULTS: This project has been pending for the past 1½ year for time and personnel to complete.

FACILITIES TO BE USED: Hematology/Oncology Clinic LAMC

FUND: None.

WORK UNIT NO. 129

TITLE OF PROJECT: The Incidence and Natural Course of Subacute Hepatitis with Bridging in Early Viral Hepatitis

INVESTIGATORS: Principal: John J. Jolley, MAJ, MC

Associate: None

OBJECTIVE: To determine what is the incidence of SHN in an unselected group of patients with acute viral hepatitis and what clinical or biochemical parameters will separate SHN from classic hepatitis.

TECHNICAL APPROACH: Project completed. 46 patients were studied. SHN occurs in 20% of our patients with acute viral hepatitis. Patients with a normal prothrombin time or negative HBsAg did not have SHN.

PUBLICATION & CONCLUSIONS: Presentation at Society for investigation of liver disease. Plan publication in Gastroenterology.

WORK UNIT NO. 130

TITLE OF PROJECT: Electroencephalographic and Body Physiological Alterations associated with successful Use of Biofeedback in the Treatment of Migraine.

INVESTIGATORS: Principal: Francis B. Buda, MAJ, MC

Associate: John M. Motl, CPT, MC

OBJECTIVE: To measure any alterations in EEG, body temperature, pulse, EKG, respirations and blood pressure which occur during the use of autodigital hyperthermia in the successful abortion of migraine attacks.

TECHNICAL APPROACH: The patient population will be cosen from that pool of individuals for whom the usual anti-migraine pharmacological agents have been tried without satisfactory control of the problem. Training in autodigital hyperthermia will occur before the patient will qualify for the study and will continue until the patient can reliably induce a rise in hand temperature of a least 2½ degrees Fareheit. The following parameters will be studied: EEG, Blood Pressure, Body Temperature, Respiration, Pulse and EKG.

PROGRESS & RESULTS: The biofeedback techniques are now being utilized as a form of therapy in patients with headache, both with migraine and muscle contraction types. This study is being undertaken to investigate what specific alterations in body physiology are important in the abortion of headaches with biofeedback as well as to determine which method of biofeedback would be most useful in the abolution of attacks of migraine and muscle contraction headache.

FACILITIES TO BE USED: EEG Laboratory LAMC.

FUND: None.

PUBLICATION & CONCLUSIONS: None.

In addition, a new treatment approach for patients with a chronic headache disorder was studied. It became apparent that there were a certain significant number of patients with chronic headaches, both vascular and musculoskeletal types, who were non-responsive to standard treatment regimens and to many alternate treatments as well. All patients entering the study were screened to rule out structural disease with a complete neurological exam, EEG, skull series, and in some cases brain scans. The patients were screened psychologically with a full diagnostic interview. The combination treatment consisted of: (1) 8 weekly 30 minute biofeedback treatment periods; (2) 8 weekly one hour group therapy periods; (3) symptom charting by patient; and (4) instruction in a form of "relaxation" exercise which was to be practiced by the patient twice daily. 14 selected patients were treated in

TITLE OF PROJECT: Electroencephalographic and Body Physiological Alterations Associated with successful Use of Biofeedback in the Treatment of Migraine

and 8 week period, using the measurement of "percentage of patients achieving greater than 50% reduction of symptoms" - 80% of the patients in this series achieved this result. In a one year follow-up period, the patients have continued to remain symptom free or significantly improved, so that the therapy appears to give long term results. The parameters utilized to assess symptoms of headaches were, frequency severity, amount of medication required, improvement in function of the patient's(job, etc).

WORK UNIT NO. 132

TITLE OF PROJECT: Effect of Hemorrhagic Shock Upon Cerebral Structure and Function

INVESTIGATORS: Principal: Michael M. Bronshvag, LTC, MC

Associates: Robert Parzynski, GS7
Charles G. Plopper, CPT,MSC
David G. Fairchild, CPT, MC
Bruce N. Persky, CPT, VC

OBJECTIVE: To determine the nature and extent of early cerebral dysfunction caused by hemorrhagic shock. To avoid artifact induced by rapid exsanguination and by effects of anesthetic agents upon the central nervous system, approximately 40 sheep were incrementally bled to the state of hemorrhagic shock. Usable data was obtained from 27. Sheep were studied with EEG monitoring, clinical monitoring (blood pressure, pulse, respiration, observation) radionuclide brainscanning and evaluation of biopsy and necropsy tissues using light microscopy, electronmicroscopy and fluorescence microscopy.

TECHNICAL APPROACH: Project completed. Manuscript has been prepared. The study demonstrated that unanesthetized sheep incrementally bled to states of hemorrhagic shock, but still awake and fully viable, had cerebral uptakes of radionuclide unaccompanied by gross leak in the blood brain barrier to Evans Blue, as measured by fluorescence microscopy. These findings were correlated with the electron microscopic finding of glial endfoot swelling, and were interpreted to demonstrate increased transport across the capillary glial interface ("blood brain barrier") rather than a destructive lesion of blood brain barrier. In addition, mitochondrial swelling was noted. Since all sheep were awake and fully viable, it was felt that mitochondrial swelling was reactive rather than a primary destructive process. This suggests that early mitochondrial changes in hemorrhagic shock, as well as in anoxic or ischemic states (such as strokes) may be reactive and not indicative of a primary lesion of mitochondria. Since cerebral mitochondria can function at partial pressures of oxygen frankly incompatible with life, it is suggested that potentially reversible derangement of cerebral neuronal structure might be caused by mitochondrial over-function, and that techniques such as barbiturate anesthesia and hypothermia may be protecting the brain by suppressing inappropriate mitochondrial over-activity. The implications of these observations for the emergency treatment of hemorrhagic shock and the interpretation of data regarding cerebral anoxic-ischemic disease from other centers is further discussed in the manuscript. EEG changes were mild and roughly reflected the clinical state of the animal, therefore adding little if anything to the clinical management of the laboratory model.

FUND: None.

PUBLICATION & CONCLUSIONS: Paper has being submitted for publication.

WORK UNIT NO. 133

TITLE OF PROJECT: Human Chorionic Gonadotropin(HCG) in the Treatment of Obesity

INVESTIGATORS: Principal: John J. Deller, COL, MC

Associates: Mark R. Stein, MAJ, MC
Ronald E. Julis, CPT, MC

OBJECTIVE: To determine if HCG is beneficial in aiding weight reduction.

TECHNICAL APPROACH: Patients were solicited for the study by advertising in the medical center bulletin. All respondents were screened by a questionnaire and each received a full explanation of the "double-blind" nature of the study and gave their informed consent to participate. They were then given a complete physical examination and a battery of laboratory tests including a complete hemogram, chemistry screen, thyroid and pituitary function tests. Each patient was assigned a number in order of their physical examination; the numbers were then randomized into two treatment groups by a registered hospital pharmacist. All patients were female and between ages 18 and 60. Patients with a history of heart disease, renal disease, asthma, gout, hypoglycemia, migraine, genital malignancy, or breast malignancy were excluded. Patients were excluded if they had: previously been treated with HCG; taken appetite suppressants in the previous 3 months; a baseline weight which was not within 10 pounds of what it had been 3 months prior to the study; a current pregnancy or were within 4 months postpartum or were nursing an infant; or been taking medications other than estrogens or birth control pills.

PROGRESS & RESULTS: Of the 51 patients starting the study, 20 of 25 in the HCG group and 21 of 26 in the placebo group completed 28 injections; there was no significant difference between the groups in the mean number of injections received. Patients #12 and #28 lost their motivation and stopped participation. Patient #55 received transfer orders. Patient #19 left on emergency leave, and #26 left on an unanticipated vacation. Patient #39 was found to have laboratory evidence of hypothyroidism and was started on thyroid replacement after receiving her 20th injection. All analyses outlined in the methods section were performed, and no statistically significant differences were found between the two treatment groups on any test. Although the direction of the differences favored the HCG group, the differences were all small and in no instance was the p value (one-tailed) less than 0.25. Ignoring effects of treatment, significant decreases (p .005) during the treatment period were seen in hematocrit, WBC, BUN, cholesterol, triglyceride, and total protein, Significant increases occurred in the fasting glucose and uric acid. Only one treatment group related difference emerged: the increase in fasting glucose appeared to be significantly greater in the placebo group than the HCG group. Both groups experienced significant downward shifts in blood pressure, but no treatment group differences were noted. Study is completed.

TITLE OF PROJECT: Human Chorionic Gonadotropin(HCG) in the Treatment of Obesity

FUND: None.

PUBLICATION & CONCLUSIONS: There is no doubt that the milieu under which this total program was administered to a highly motivated group of women can be and was successful in achieving rapid weight reduction. But HCG per se offered no advantage over placebo injections in this setting in regard to weight lost, distribution of fat lost, or hunger index during weight reduction. Our data to date can not answer the question of safety. Additional studies are underway to address this question. We also have not resolved why our data refutes that reported by Asher and Harper but point out potential areas which may account for the differences. This study was performed in a manner similar enough to current treatment programs based on the Simeon's technique for weight control to disprove any inherent efficacy of HCG in these programs.

WORK UNIT NO. 133(2)

TITLE OF PROJECT: Immunologic Surveillence of Obese Pts Receiving Human Chorionic Gonadotrophin(HCG) in Conjunction with Dietary Restrictions for Weight Reduction in a Double Blind Study: An Addendum to Protocol Entitled "Human Chorionic Gonadotrophin(HCG) in the Treatment of Obesity".

INVESTIGATORS: Principal: William H. Stone, MAJ, MC

Associates: Glen Justice, MAJ, MC
Josephine Polakoff, GS7

OBJECTIVE: To ascertain if low dose in vivo HCG causes suppression of T Cell(lymphocyte) function as measured by blast transformation using PHA, and specific antigens.

TECHNICAL APPROACH: All patients entered on the LAMC Obesity study utilizing HCG will have the following tests performed: T-Cell numbers will be determined by subtracting fluorescent lymphocytes (B-cells or immunoglobulin producing lymphocytes) from other blood elements using ficol-hypaque centrifugation and staining the living lymphocytes with polyvalent anti-immunoglobulin. Total T-Cell rossettes will also be determined using sheep red blood cells. T-cell function, as measured by PHA stimulation of lymphocyte transformation using ^{14}C thymidine incorporation as a label, will be determined. T-cell function toward specific antigens, as measured by mumps and candida antigen stimulation of lymphocyte transformation using ^{14}C thymidine incorporation as a label, will be determined. In vivo cell mediated immunity will be observed using skin test reactivity to mumps and candida antigens before and at the end of HCG administration. Approximately 20cc of heparinized whole blood would be drawn, along with other studies outlined in the obesity protocol, prior to beginning HCG injections and one day after the last HCG injection.

PROGRESS & RESULTS: Work has continued on the invitro charateristics of HCGs effect upon T-lymphocyte function. Data is presently being statistically analyzed for future guidance and protocol design.

FACILITIES TO BE USED: Hematology/Oncology Clinic and Clinical Investigation Service's Laboratory LAIR.

FUND: Consumables $5,213.47 MEDCASE $1,450.00

PUBLICATION & CONCLUSIONS: None

WORK UNIT NO. 136

TITLE OF PROJECT: Plasma Exchange in the Treatment of Immune Disease

INVESTIGATORS: Principal: William H. Stone, MAJ, MC

Associates: Glen R. Justice

OBJECTIVE: Plasma exchanges in patients with life threatening problems due to immunity complications (complex, AB etc) to remove the offending complex or AB.

TECHNICAL APPROACH: Study patient population will be drawn from LAMC other local military hospitals, and the San Francisco VA hospital. Patients with autoimmune disease who are having problems related to the presence of antibodies which if successfully removed could cause a remission in the patients clinical condition will be candidates for plasma exchange on this protocol. Such patients will first have to be shown to be resistant to more conventional therapy or the risks of conventional therapy will have to be adjudged excessive when compared to the risks of plasma exchange.

PROGRESS & RESULTS: Patients have not been placed on this protocol during the past 1 year, however it is the desire of the investigator to have it remain open so that when a suitable case is present, the protocol can be utilized.

WORK UNIT NO. 137

TITLE OF PROJECT: The Earlobe Crease - A Microscopic Study

INVESTIGATORS: Principal: Richard J. McCarty, COL, MC

Associate: Herbert D. Brahman, MAJ, MC

OBJECTIVE: To determine whether or not there is any histologic abnormality present in the earlobes of patients with creases as contrasted with the uncreased earlobe.

TECHNICAL APPROACH: Earlobes will be assessed clinically as to presence or absence of creases. Photographs of each earlobe will be obtained. Biopsies will be performed after appropriate informed consent is given. In autopsy specimens correlation will be made with the presence of arteriosclerosis of the coronary arteries which will be graded according to number of vessels involved as well as degree of obstruction. Small intramyocardial branches of coronary arteries will be examined microscopically as well. Living patients will be assessed for presence of earlobe crease. Presence of ASHD will be listed as confirmed by prior myocardial infarction, positive stress test and/or coronary angiography. Coronary angiography will be performed only when indicated for clinical reasons. Earlobe biopsies will be performed by plastic surgery service after obtaining appropriate informed consent. Diabetes mellitus will be sought with standard blood glucose screening tests. Tissue obtained from all patients will be examined histologically. Control group shall be autopsy specimens without earlobe crease.

PROGRESS & RESULTS: Second specimen is under study by the Pathology Service. Cadover will be studied. Biopsy will not be done on patients.

FACILITIES TO BE USED: Pathology Service LAMC

FUND: None required.

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 138

TITLE OF PROJECT: A Clinical Trial of Timolol Maleate in the Treatment of Hypertension

INVESTIGATORS: Principal: Thomas J. Egan, LTC, MC

Associates: Paul Killiam, CPT, MC
Helen Rutledge, MAJ, ANC

OBJECTIVE: To find if timolol maleate is effective, safe and well-tolerated when used in the treatment of hypertension in a twice-daily dosage regimen.

TECHNICAL APPROACH: The study will be limited to outpatients of either sex between the ages of 21 and 65 years with mild to moderate uncomplicated essential hypertension. Each patient is to be assigned to one of two strata as defined by their untreated diastolic blood pressure. Stratum I will consist of patients with an untreated diastolic blood pressure of from 95 to 105 mm Hg. Stratum II will consist of patients with an untreated diastolic blood pressure offrom 106 to 115 mm Hg.

PROGRESS & RESULTS: Approximately 80% of the subjects have completed their trial of timolol. They will return for a follow-up examination. The remainder of the subjects have 12-20 weeks to go.

FACILITIES TO BE USED: Ambulatory Internal Medicine Clinic and Laboratory LAMC.

FUND: None required by LAMC.

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 139

TITLE OF PROJECT: Cognitive Set Hierarchies in Aphasia

INVESTIGATORS: Robert A. Kaplan, CPT, MS

Gary G. Balestin, MA, VAH Palo Alto, CA

OBJECTIVE: To investigate which of the cognitive sets already established in various populations are present in aphasic patients; by so doing, it may be possible to assess the relationship between throught and language.

TECHNICAL APPROACH: Aphasic patients will be selected from the Neurological Service and Speech Pathology Service of LAMC. They are to be righthanded, with English as their original language, between the ages of 45 and 65 years, non-psychotic and without evidence of other neurological disease. Etiology of aphasia is to be a cerebrovascular accident, at least 3 months but less than 4 years post trauma. Experimental and control subjects will be individually administered a 60-word free association test. All subjects will be told that they are to listen to the word the examiner will say, and are to then respond with the first word or idea which comes to mind. All responses will be recorded, as will reaction time. Responses will be clerically scored according to preselected categories, e.g., synonym, coordinate, etc. The time involved will be approximately 15 minutes for each individual.

PROGRESS & RESULTS: 35 male aphasic patients diagnosed by experienced speech clinicians were selected from the neurological wards of regional military and county hospitals and private hospitals. 15 patients were selected who were classified as semantic, 15 who were classified as syntactic and five who were classified as pragmatic aphasics according to the criteria for these clinical types by Wepman. The aphasic population was unusually homogenous in terms of lesion site, etiology, pre-trauma language ability, months post-trauma at time of testing, and age and education. A matched control group of 30 non-aphasic subjects was selected from the non-neurological wards of the same institutions. Each subject was individually administered a 60 item word association task under three conditions: (1) auditory presentation of the stimuli, (2) visual presentation of the same stimuli, and (3) visual presentation of the same stimuli but with a listing of possible associates provided. In the last procedure, subjects were required to select what they considered an appropriate associate. Stimuli were randomized as much as possible within the factorial design. A period of from seven to ten days separated each experimental condition. The stimuli were selected from the published association norms. Associations were scored according to one of nine semantic/logical categories, as well as other variables such as frequency and imagery. All scoring was clerical; there were two scorers. Results suggested that semantic aphasic language is quantitatively different from non-aphasic language; an hypothesized impaired selection mechanism intervening between an intact, holographically organized

TITLE OF PROJECT: Cognitive Set Hierarchies in Aphasia

memory system and a cognition-structuring system was proposed to account for the different in processing efficiency. Semantic aphasia was also considered a unidirectional impairment. Syntactic aphasic language was considered qualitatively different from non-aphasic language; the difference was most evident in the higher percentage of syntagmatic associates. The language of the pragmatic aphasics was considered to reflect both a qualitative and quantitative difference due primarily to intellectual deficit and an impaired selection mechanism. There were indications of modality specific impairments for each type of aphasia. The varimax factor solutions of the association categories supported the position that semantic aphasic is linguistically and cognitively closer to non-aphasic speech and cognition than in syntactic aphasia, contrary to theory.

FACILITIES TO BE USED: Psychology Service Ward, LAMC and Psychology Service VAH Palo Alto, CA

FUND: None required

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 140

TITLE OF PROJECT: Effect of Oral Phosphate on VER in Multiple Sclerosis

INVESTIGATORS: Principal: Roby P. Joyce, CPT, MC

Associate: William W. Campbell, Jr., MAJ, USAF, MC

OBJECTIVE: To assess effect of induced hypocalcemia on the latency and configuration of the VER in patients with demyelinating optic nerve disease.

TECHNICAL APPROACH: VER equipment for this study has only recently been set up and therefore no progress has been made.

WORK UNIT NO. 141

TITLE OF PROJECT: Comprehensive Viral Immunology of Multiple Sclerosis

INVESTIGATORS: Principal: Michael M. Bronshvag, LTC, MC

Associates: Kenneth P. Johnson, VAHSF
Jerry S. Wolinsky, VAHSF
Richard Baringer, VAHSF
Lynn Spitler, UCSF

OBJECTIVE: To measure antibody titers to multiple viruses in CSF and serum of MS patients and controls. Studies of cellular immune reactivity to brain and viral antigens will be performed. Such studies will be repeated at 3-6 month intervals to compare several immunological parameters to each other and to clinical disease activity.

TECHNICAL APPROACH: Groups studied: (1) patients with typical MS i.e., a CNS disease beginning in young adults life caracterized by exacerbations and remissions and associated with increase in IgG in the CSF. (2) patients with presumptive or atypical demyelinating disease such as those with optic neuritis (30% later develop MS) or chronic myelitis (some of whom have MS lesions pathologically). (3) controls - age and six matched patients undergoing:(a) neuroradiological procedures (myelography, pneumoencephalography), (b) neurological evaluation for diseases other than MS where a lumbar puncture is diagnostically indicated. Procedures: Viral antibodies studies - serum and CSF will be assayed for measles, rubella, vaccinia, herpes, mumps, cytomegalovirus and influenze antibodies. CSF will be concentrated and analyzed by agarose electrophoresis for oligoclonal collections of immunoglobulins. Cellular immune assays - fresh lymphoctyes will be assayed for reactivity to CNS basic protein and measles, rubella, mumps, vaccinia and perhaps other viral antigens. Leukocyte migration and lymphocyte stimulation tests will be used.

PROGRESS & RESULTS: 8 patients have been evaluated. In seven, three of whom probably or definitely had multiple sclerosis, results were negative. In one (study #2096) oligoclonal banding was detected. Subsequent autopsy of this patient was compatible with cerebral vasculitis and meningitis, etiology unknown, magnitude mild. The findings were not compatible with either multiple sclerosis or his clinical diagnosis(Jacob-Crutzfield). The significance of this finding is being evaluated.

FACILITIES TO BE USEl: LAMC and laboratory at University of California San Francisco or University of California Berkeley.

FUND: None required.

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 142

TITLE OF PROJECT: Standardization of Hypoglycemic Criteria Using a Physiologic Stimulus

INVESTIGATORS: Principal: Harvey L. Eichner, LTC, MC

Associate: M. Arthur Charles, LTC, MC

OBJECTIVE: To establish criteria defining normal postprandial blood glucose and glucoregulatory hormone concentrations following a test meal which provides more physiological stimulus than pure glucose and to compare these data with the traditional oral glucose tolerance test. Also to observe whether patients thought to have idiopathic reactive hypoglycemia do in fact have low postprandial blood glucose and altered levels of glucoregulatory hormones associated with clinical findings following the test meal.

TECHNICAL APPROACH: Normal volunteers: A pilot study of 10 male and 10 female subjects of ideal body weight, between the ages of 20-50, who have no discernable medically relevant conditions which would interfere with the study, will be evaluated. A pilot study of 10 patients of ideal body weight (ages 20-50) presenting to LAMC clinics with a syndrome compatible with the diagnosis of IRH will be evaluated. If the pilot study indicates that IRH is or is not related to blood glucose, the number of normal subjects and patients will be increased 50 each. An oral glucose challenge (40 gm/M^2) will be administered following 3 days of the subject's usual diet which will be adjusted to contain 150 gm of carbohydrate (10). The glucose solution will be taken at 0800 hrs after a 12 hour fast and patients are to be instructed to forego vigorous exercise, cigarette smoking or caffeinated beverages before and during the test. All patients will be studied in the sitting position and the osmolar load will be similar in all cases.

PROGRESS & RESULTS: Project terminated due to transfer of responsible investigator. Data have been collected on 11 patients and normals. Since the number of subjects was too small no valid conclusions could be reached.

FUND: None.

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 143

TITLE OF PROJECT: Comparison of Percutaneous Liver Biopsy and Cytology with Biopsy Obtained at Peritoneoscopy in the Diagnosis of Metastatic Carcinoma of the Liver

INVESTIGATORS: Principal: Gregory E. Craner, MAJ, MC

Associates: Kress Lockridge, LTC, MC
Melvin L. Butler, LTC, MC

OBJECTIVE: To determine whether peritoneoscopy with directed liver biopsy add significant positive findings in the evaluation of metastatic liver disease.

TECHNICAL APPROACH: Due to lack of personnel, the project has been terminated.

WORK UNIT NO. 144

TITLE OF PROJECT: An Evaluation of the Efficacy of Tadenan in the Treatment of Benign Prostatic Hyperplasia

INVESTIGATORS: Principal: Ray E. Stutzman, COL, MC

Associates: Jack W. McAninch, LTC, MC
Lloyd J. Peterson, MAJ, MC

OBJECTIVE: To test the effects of a medication on the relief of symptoms of benign prostatic hyperplasia.

TECHNICAL APPROACH: The FDA has temporarily withdrawn approval after it was ascertained that if Tadenan was approved for the US market, the natural component of the drug would not adequately supply pharmaceutical needs in this country. Therefore, the active synethic ingredient of the drug was undergoing further Phase II testing before it will be ready for clinical research. Conversations with the Research Director indicates that it will probably be another two or three months before the drug will be available for Phase III study at this institution.

WORK UNIT NO. 147

TITLE OF PROJECT: Multicenter Retrospective Study on Replacement Therapy of Menopausal Hormonal Deficiency and Incident of Carcinoma of the Endometrium and Breast

INVESTIGATORS: Principal: John J. Deller, Jr., COL, MC

Associates: Sam Hull, MAJ, MC
Eldridge Piersal, MAJ, MC

OBJECTIVE: Recent reports have suggested a causal relationship between the occurrence of endometrial carcinoma and estrogen therapy in post-menopausal females. The objectives of this study are to determine if therapy with estrogenic agenst is a risk or benefit factor for endometrial carcinoma(ECa) or breast cancer (B Ca); if combined estrogenic progestational therapy affects the risk; if duration and/or dosage and continuous versus cyclic therapy affects the risk; if family history, gynecologic history, race, parity, blood pressure, weight, or other medications or illnesses would help to identify those patients at greater risk.

TECHNICAL APPROACH: A pilot study has been undertaken utilizing inpatient medical records from LAMC and David-Grant US Air Force Medical Center under the diagnostic codes of carcinoma of the endometrium and carcinoma of the breast for the years 1970-1975. It has been decided to pursue a comprehensive retrospective analysis of all medical records of women over 40 years of age under these diagnostic codes from 1 Jan 1970-31 Dec 1975 from the seven US Army Medical Center facilities and David-Grant US Air Force Medical lenter, and Oak Knoll Naval Medical Center. Inpatient medical records, on patients whose names will be provided by the hospital Tumor Registries, will be requested through patient administrative channels from LAMC to the aforementioned medical centers. Medical records of the study cases will be programmed to be received at time intervals that would allow analysis of an individual hospital's records within a two-week time-frame so that these records would not be out of circulation for more than 30 days. For controls, each of the medical centers will be asked to provide a chart of a female patient hospitalized during the same 3-month period as the indexed case on either the OB-GYN or Surgical Service for a non-cancerous surgical procedure. The controls will be matched for age within one year, parity within one child, weight within 20 lbs and race.

PROGRESS & RESULTS: Review of charts from four medical centers has been completed. 146 cases of ECa (plus controls) and 293 cases of BCa (plus controls) have been reviewed. No statistical analysis of data has been completed. The study is being done in collaboration with personnel from Department of Medicine, Letterman Army Institute of Research, R&D Command.

FACILITIES TO BE USED: Department of Medicine LAMC.

FUND: Approximately $800 funded by HSC for computer time and keypunch operator time.

PUBLICATION & CONCLUSIONS: Recent publications have suggested that treat-

TITLE OF PROJECT: Multicenter Retrospective Study on Replacement Therapy of Menopausal Hormonal Deficiency and Incidence of Carcinoma of the Endometrium and Breast.

ment of post menopausal hormone deficiency with estrogenic agents is associated with an increased risk of ECa. A retrospective analysis of hospital charts from seven military medical cneters (years 1970-1975) of all patients with the initial diagnosis or treatment of ECa or BCa is being done. Military medical records are particularly suited for this study because of the duration of record keeping, uniformity of records, availability of records and because many pathological diagnoses are reviewed at the AFIP.

WORK UNIT NO. 148

TITLE OF PROJECT: Prevalence of Asymptomatic Neurosyphilis

INVESTIGATORS: Principal: Daniel C. Traviesa, MAJ, MC

Associate: Stephen Prytowski, MAJ, MC

OBJECTIVE: To determine the incidence of CSF abnormalities suggestive of syphilis in asymptomatic patients with reactive serum serology and either no history of treatment or history of inadequate treatment.

TECHNICAL APPROACH: Patients over 30 years of age reporting to AIM Clinic for routine physical examination only, will receive a serum VDRL and FTA-ABS test. The number of patients tested will be limited to 15 per week. A complete history and physical examination will be performed. A complete history for past venereal disease and treatment will be obtained. Patients who have undergone adequate therapy for syphilis and have no evidence of recurrence on examination will be referred back to the primary physician. Should any patient have evidence of primary or secondary syphilis, he will be referred for immediate admission, work-up and therapy. Patients with reactive FTA-ABS and no history of syphilis or history of inadequate treatment(i.e., heavy metals, incomplete antibiotic regimen, etc) for known syphilis will be told that they were probably exposed to syphilis sometime during their life and that further testing of the spinal fluid and eventual prophylactic therapy with antibiotics is indicated.

PROGRESS & RESULTS: Approximately 200 patients reporting to the AIM Clinic for routine physical exam only have received a serum VDRL and FTA-ABS test. 15 of these patients have had a reactive FTA-ABS. Five of these 15 patients had a reactive serum VDRL. One patient was lost to follow-up. Three patients had a history of syphilis with inadequate treatment. Eight patients have had no history of syphilis. Of these 11 patients eligible for further investigation according to the protocol, seven have had complete work-ups, two have an ongoing work-up at present and two have work-ups that are pending. Repeat FTA-ABS tests were performed on these patients with a consistent reactivity in all. Samples of the same specimen were sent to WRAIR Immunology Branch for FTA-ABS and TPI tests. The FTA-ABS was reactive in all samples sent and the TPI was reactive in four of the seven samples tested so far. History and physical examination and serum tests, as outlined in protocol, looking for possible markers of false positive reactors, have been negative in all patients tested. Of the eight patients undergoing complete CSF evaluation, only two have demonstrated any CSF abnormality. The presence of oligocloncal CSF bands were noted in both suggesting the presence of chronic inflammatory disease of CNS. In one, a mild increase in the CSF IgG gamma globulin was also noted. All other tests on CSF(T. P., cells, culture, VDRL, glucose) were normal. Election of these oligocloncal bands and determination of their possible specific FTA reactivity are pending.

FACILITIES TO BE USED: AIM Clinic, Neurology Clinic, Dermatology Clinic LAMC and Fort Baker Serology Laboratory.

FUND: None required.

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 150

TITLE OF PROJECT: Clinical Uses of a Portable Hand Held Magnetic Cassette Videotape System

INVESTIGATORS: Principal: Michael M. Bronshvag, LTC, MC

Associate: Daniel Haug, GS7

OBJECTIVE: To evaluate the potential of a hand held video cassette recorder-player generate medical records comparable to standard clinical charts. Since doctors' memories can be short, written records occasionally misleading and expert consultation temporarily unavailable, a film record on a 60 minutes magnetic video cassette (price $33.00) may be valuable in followup and continued treatment of individual patients.

TECHNICAL APPROACH: Informed consent will be obtained in coherent patients, and approval of guardians for minors and incompetents. Since the use of this technique is primarily to store data to enhance patient care by the primary MC, comatose and delerious patients can be used. Each patient will be examined by the investigator and the regular LAMC team. Since the investigator is a fully trained specialist, his primary interest will be in meeting the patient's health care needs. Appropriate records will be reviewed and the investigator will submit a standard consultation. Appropriate parts of history and examination will be filmed. Sequential film clips will either be recorded on a single cassette or called onto a single cassette. Film will be reviewed when appropriate for medical care and this will be the basis for the study.

PROGRESS & RESULTS: Several patients with interesting or challenging findings have been recorded. In one, the clinical course of hand causalgia unresponsive to percutaneous sympathetomy but subsequently responsive to re-exploration of the injuried nerves was documented. In another, course of asterixis secondary to a head injury was documented and followed. Although further experiences required, it is felt that the video camera setup is making a contribution to clinical care of individual patient as well as being a tool for clinical teaching. The investigator plans in the coming year to especially search for cases in which demonstration to an expert consultant of a video cassette resulted in diagnostic or therapeutic suggestions valuable in that patient's management.

FACILITIES TO BE USED: Ward LAMC

FUND: Equipment: $6371.88

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 500

TITLE OF PROJECT: Longitudinal Follow-up of High Risk Babies by Means of Auditory Evoked Responses

INVESTIGATORS: Principal: Philip G. Pettett, MAJ, MC

Associate: Charles M. McKean, MD

OBJECTIVE: To define the maturational pattern of the neonatal brainstem reflex responses to an auditory stimulus in a longitudinal fashion. In addition anoxic or asphyxiated infants will be studied and clinical correlation will be made to determine prognostic and diagnostic values for this test.

TECHNICAL APPROACH: Neonates will be placed in bassinets or radiant heaters as dictated by their condition. An active electrode (Grass, silver disc) is placed at the vertex (Zc) of the scalp and referred to either earlobe (A1 or A2). The forehead serves as the ground site. The electroencephalogram is led into a Grass P-511 preamplifier, set to pass a signal between 10 Hertz (Hz) and 3 kilohertx (kHz) (0.5 amplitude range) with a gain of $1x10^6$. The stimulus consists of brief (50 microsecond) clicks, driven by a Grass SD9 stimulator and delivered binaurally through a head set (Realistic 10 LV). The intensity of the stimulus is approximately 60 decibels above sensation threshold (experimenter's sensation level). This stimulus is the minimum output necessary to show an adequate electroencephalographic response from the brainstem. The term sensation level refers to the intensity in decibels of the signal above threshold. This measurement is recalibrated each time the equipment is utilized since zero decibel sensation level depends on such variables as the particular earphone used and the sound level of the environment in which the testing is done. The click stimulus is calibrated by using a sound level meter. A voltage attenuator is set at the 60 decibel sensation level and the voltage output is measured with the oscilloscope. This applies uniform voltage each time the equipment is used. Brainstem potentials evoked by up to 2400 stimuli are automatically summated on line with a computer of average transients (TMC 1000 C) and graphically displayed on an X-Y plotter.

PROGRESS & RESULTS: Enrollment of patients in the auditory evoked response study has been underway for approximately 1½ months. At this time 30 patients have been collected in the normal group and five in each of the abnormal groups. All enrolled patients have had their initial evaluations done and are at various stages of progress in the follow-up studies in Well Baby Clinic. No attempt has been made at this time to analyze any of the data. This will be done only as specific groups are completed at each time interval of testing. There have been no major problems in patient compliance with the testing and parents have been very willing to participate in this study. Data will be analyzed by the early part of September or October.

TITLE OF PROJECT: Longitudinal Follow-up of High Risk Babies by Means of Auditory Evoked Responses

FACILITIES TO BE USED: LAMC Newborn Nursery and Newborn Intensive Care Unit

FUND: MEDCASE $5,000.00

PUBLICATION & CONCLUSIONS: None

WORK UNIT NO. 501

TITLE OF PROJECT: Pediatric Enteropathogen Study

INVESTIGATORS: Principal: Frank W. Crast, MAJ, MC

Associates: S. Vern Juchau, MAJ, MSC
James L. Stewart, Jr., COL, MC
Creed Smith, LTC, MSC

OBJECTIVE: To delineate the clinical spectrum of several gastrointestinal agents in pediatric patients. The agents are to include Salmonella sp., Shigella sp., Enteropathogenic E. Coli sp., Yersinia sp., Edwardsiella tarda(non-cholera) Vibrio sp., including Vibrio parahemolyticus and also a survey of viral agents as related to gastrointestinal signs and symptoms. Comprehensive medical care is provided to all military dependents. Diarrhea and other gastrointestinal signs and symptoms constitute a significant health problem in the pediatric age groups here and especially in developing countries where we have military interests. It was one of the five most common reasons for admission to the Pediatric Medical Ward, LAMC, in 1974-1975, comprising 10% of 485 admissions. It represents 1-30% of Pediatric Clinic visits per day for the same time period.

TECHNICAL APPROACH: Children presenting to the Pediatric Clinic, LAMC, with acute and/or chronic gastrointestinal symptoms will be eligible for the study unless the child has been placed and is on antibiotic therapy or where the symptoms clearly relate to a non-infectious agent or etiology, i. e., Theophylline induced nausea. Controls will be patients presenting for non-gastrointestinal problems. Control patients will be chosen by age to match their counterpart ill patient(i.e., EPS 21A, the control, will match EPS 21B and their age will be comparable). All children entered on the study will get acute and convalescent serums for viral titers to include Adenovirus, Influenza, Parainfluenza, RS virus, Echo, Polio, Coxackie and CMV. Acute and convalescent sera will also be saved for evaluation for CF titers for Yersinia, Vibrios, Edwardsiella and any other viral and non-viral agents that may be grown in stool cultures.

PROGRESS & RESULTS: This study started at a trial rate of approximately two specimens being processed per week. Stool specimens had Serotype pos Enteropath E. coli - 1 Echo 6 virus. Viral Isolation - 1 Polio 3 vacc Strain. An article in the July 1976 Journal of Pediatrics demonstrated that serotyping of E. coli is invalid and that Adrenal Cell, suckling mice and guinea pig enteropathogenic tests for heat labile toxin, heat stable toxin and enteroinvasiveness respectively are the most accurate assessment for pathogenesis of E. coli.

FUND: $4,782.75.

FACILITIES TO BE USED: Department of Pediatrics Clinic and Fort Baker Medical Laboratory.

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 302

TITLE OF PROJECT: Gallium^{67} Citrate for Diagnosis of Malignant Neoplasms and/or Abscess Localization

INVESTIGATORS: Principal: Ralph Blumhardt, LTC, MC

Associates: Less Chafen, LTC, MC
David L. Yuille, MAJ, MC
Alton W. Baker, LTC, MC
Gary G. Shrago, MAJ, MC

OBJECTIVE: To evaluate the clinical efficacy of Gallium-67 Citrate.

TECHNICAL APPROACH: Project terminated.

PROGRESS & RESULTS: Gallium-67 citrate has new drug approved for routine use by the USFDA, therefore the study has been terminated. Gallium has been found to be safe and effective. There were no patient side effects and no publications.

FUND: None.

WORK UNIT NO. 306

TITLE OF PROJECT: Clinical Evaluation of the Thyroid by invivo Radionuclide Studies Utilizing I^{123}

INVESTIGATORS: Principal: Robert Lull, LTC, MC

Associate: David L. Yuille, MAJ, MC
Brent Kehn,LTC, MC
Hebert W. Henry, MAJ, MC
Robert Telepak, MAJ, MC

OBJECTIVE: To determine if 123_I can be substituted for 131_I for thyroid scanning and thyroid uptakes.

TECHNICAL APPROACH: Approximately 100 uCi 123_I is administered orally and a thyroid uptake and scan are performed at 24 hours. Quality control checks are performed on the administered 123_I to access radiopurity.

PROGRESS & RESULTS: Approximately 700 patients have received 123_I at LAMC without any observed reactions. Correlation of scan findings and 24 hour RAIU with clinical data reveals essentially the same correlation as would be expected with I^{131}. As the radiation exposure to the thyroid from 123_I is less than 5% of the radiation exposure from 131_I, the use of 123_I is felt to be highly desirable.

FACILITIES TO BE USED: LAMC Nuclear Medicine Service.

FUND: None.

PUBLICATION & CONCLUSIONS: a. 123_I should be made a routine radiopharmaceutical to reduce patient radiation exposure with no loss in diagnostic information in thyroid uptakes and scans. b. Publication - none.

WORK UNIT NO. 308

TITLE OF PROJECT: Clinical Evaluation of Renal Cortical Imaging Utilizing 99mTc-Kidney Scintigraphin-(2,3-dimercapto Succinic Acid)

INVESTIGATORS: Principal: David L. Yuille, MAJ, MC

Associates: Robert Lull, LTC, MC
Brent Kehn, LTC, MC

OBJECTIVE: To evaluate the usefulness of 99mTc DMSA as a renal cortical scanning agent, in studying renal anatomy and blood flow in normal and pathologic kidney. The agent may also be evaluated as an agent for studying renal function.

TECHNICAL APPROACH: Following the IV administration of 5mCi of 99mTc DMSA a rapid sequence renal blood flow study is obtained. Static images of the kidneys are then taken after a 2-3 hour delay using a pinhole collimator. Posterior views as well as both oblique views are obtained of both kidneys. When possible, the results will be correlated with clinical data, IVP's, sonography, and arteriography.

PROGRESS & RESULTS: To date approximately eight studies have been carried out at LAMC utilizing this agent. No adverse reactions to this agent have been encountered. In the few cases done, results have been similar to 99mTc-Sn-gluconate(see report on 99mTc-Sn-gluconate). Few cases have been done at LAMC with this agent because results using 99mTc-Sn-gluconate are generally excellent, and the cost of DMSA is considerably higher than gluconate. However, in the two cases when patients were studied with both DMSA and gluconate, the results with DMSA were equal to or better than that with gluconate. Becuase the investigative protocol limits the dose to 5mCi, flow studies with the agent have been poor.

FACILITIES TO BE USED: Nuclear Medicine Clinic LAMC

FUND: None

PUBLICATION & CONCLUSIONS: a. Recommend continued gathering of cases done with both DMSA and gluconate for further comparison. b. Recommend raising the dose limit of 99mTc DMSA to 15mCi to allow the performance of adequate flow studies. c. Publications - none.

WORK UNIT NO. 309

TITLE OF PROJECT: Clinical Evaluation of 99mTc-Sn-Gluconate as a Kidney Imaging Agent

INVESTIGATORS: Principal: David L. Yuille, MAJ, MC

Associates: Robert Lull, LTC, MC
Brent Kehn, LTC,MC
Less Chafen, LTC, MC

OBJECTIVE: To evaluate the usefulness of 99mTc-Sn-gluconate a renal cortical scanning agent, in studying renal anatomy and blood flow in normal and pathologic kidney. The agent may also be evaluated as an agent for studying renal function.

TECHNICAL APPROACH: Following the IV administration of 5mCi of 99mTc-Sn-gluconate, a rapid sequence renal blood flow study is obtained. Static images of the kidneys are then taken after a 2-3 hour delay using a pinhole collimator. Posterior views as well as both oblique views are obtained of both kidneys. When possible, the results will be correlated with clinical data, IVP's, sonography, and arteriography.

PROGRESS & RESULTS: Approximately 80 patients have been studied to date with 99mTc-Sn-gluconate. No side effects have been observed in any of these patients. A review of the first 67 renal cortical scans in 62 patients has been performed. 63 of the scans were done with 99mTc-Sn-gluconate and four were done with DMSA. There were two studies done with both DMSA and gluconate. The result of these scans were compared to IVP's sonography and arteriography. In comparison with ultrasonography, renal cortical scanning appeared to be about 50% more sensitive than ultrasound in detecting renal cortical defects, and 33% more sensitive than the IVP. However, the IVP picked up three central renal lesions which were missed on the scan. There was 100% correlation between the results of renal scanning and arteriography in 14 lesions and four normal cases. Comparison with nepheotonography revealed complete correlation in two lesions and two normal cases. Based on this review, the normal anatomy of the kidney is felt to be understood, some anatomic variants have been observed, and criteria for abnormal studies have been developed.

FACILITIES TO BE USED: Nuclear Medicine Clinic LAMC

FUND: None

PUBLICATION & CONCLUSION: a. From this study we recommend that 99mTc-Sn-gluconate be made a routine radiopharmaceutical. b. The dose administered to patients must be raised from the study limit of 5mCi to 20mCi. The increased dose is necessary to obtain good renal flow studies. In addition, because a pinhole collimator is used and six static views are obtained, each study involves over one hour of imaging time. Thus, patient motion becomes a limiting factor in the image quality. By increasing the administered dose, imaging time can be decreased, thus increasing the image quality and making

TITLE OF PROJECT: Clinical Evaluation of 99mTc-Sn-Gluconate as a Kidney Imaging Agent (Cont'd)

the study more practical. c. The results of this study been presented in a talk at the 1976 Current Concepts in Radiology at LAMC. d. A forthcoming paper is under serious consideration.

WORK UNIT NO. 310

TITLE OF PROJECT: Myocardial Perfusion Scanning with Radioactive Particles

INVESTIGATORS: Principal: Robert Lull, LTC, MC

Associates: David L. Yuille, MAJ, MC
George Dunson, MAJ, MS
Brent Kehn, LTC, MC
Robert Telepak, MAJ, MC
Herbert W. Henry, MAJ, MC

OBJECTIVE: To evaluate myocardial perfusion during angiography with 99mTc MAA and 131_I MAA injected into the coronary arteries.

TECHNICAL APPROACH: Two mCi of 99mTc MAA will be injected into the(L) coronary circulation 10 minutes after the last prior injection of radiographic contrast material. The number of particles injected will be limited to 800,000 and/or 0.5 mg albumin. Following this, 100uCi 131_I MAA will be injected into the (L) coronary artery within 15 seconds of an injection of radiographic contrast material (which causes vasodilatation). The amount of 131_Ialbumin injected will be limited to .5mg.Following completion of the coronary arteriogram, the patients heart will be imaged in the anterior, LAO, and L lateral projection in both the 99mTc window, and the 131_I window.

PROGRESS & RESULTS: Three patients have been injected with the above technique. The first patient demonstrated normal (L) coronary circulation. Difficulty was experienced with the last patient when air was injected into the coronary arteries along with the labelled particles. The patient went into ventricular tachycardia, but recovered. Further work has been delayed until a better injection technique is devised.

FACILITIES TO BE USED: LAMC Cardial Catheterization Laboratory and Nuclear Medicine Service.

FUND: $2,207.96

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 311

TITLE OF PROJECT: Development of a Method for Enhancing Scintigraphic Images by Computer

INVESTIGATORS: Principal: David L. Yuille, MAJ, MC

Associates: Robert Lull, LTC MC
Sheldon R. Kiser, PhD

OBJECTIVE: To allow more accurate diagnosis to be made using nuclear medicine techniques by improving the image quality of nuclear medicine studies with a digital computer.

TECHNICAL APPROACH: This project will ential writing computer programs to simulate image degradation by noise and the imperfect imaging characteristics of a gamma camera. Programs will then be written to recover as much information as possible utilizing established fourrier techniques and regression analysis. Once the appropriate programs have been developed, they will be used on data derived from patients undergoing standard nuclear medicine imaging procedures to test the algouthm in clinical settings. It is to be emphasized that data collection will in no way degrade the quality of the routine studies or entail any risk of discomfort to the patient being studied.

PROGRESS & RESULTS: No progress has been made in the past year on the basic problem of image recovery. The reason for this delay is simple: The equipment needed for this project has not yet been fully operative. In August 1975, the computer which was to have been used for this project was discovered to have several serious electronic problems. These electronic malfunctions took four months to repair. However, before a component necessary to this project (a Versatec Plotter) could be installed on the computer, an expansion classic had to first be added to the system. The expansion classic is currently being installed.
Apart from the above hardware problems, several software problems have been encountered. To simulate noise requires a random number generator, and to do regression analysis requires a matrix inversion routine. Sources for both of these routines have been located. Thus all of the basic hardware and software necessary for the continuation of this project should be ready within the next month. Progress should then depend upon the time available to the chief investigator.

FACILITIES TO BE USED: Nuclear Medicine Service LAMC

FUND: None

PUBLICATION & CONCLUSION: None

WORK UNIT NO. 313

TITLE OF PROJECT: Clinical Evaluation of Cisternography Utilizing ^{111}Indium DTPA (DiethyleneTriamine Penta Acetic Acid)

INVESTIGATORS: Principal: Robert Lull, LTC, MC

Associates: David L. Yuille, MAJ, MC
Brent Kehn, LTC, MC
Herbert W. Henry, MAJ, MC
Robert Telepak, MAJ, MC

OBJECTIVE: To evaluate the clinical utility of cisternography utilizing ^{111}Indium DTPA.

TECHNICAL APPROACH: 2mCi ^{111}Indium DTPA are injected into the lumbar subarachnoid space through a spinal needle. Images are obtained of the spine at 2 hours, and of the head in the AP and lateral projections at 3,4,8,24, 48 and if necessary 72 hours.

PROGRESS & RESULTS: To date approximately 20 patients have undergone this procedure without any adverse affects. However, the number of cases collected so far is insufficient for any conclusion to be drawn about the procedure.

FACILITIES TO BE USED: Nuclear Medicine Service LAMC.

FUND: None.

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 314

TITLE OF PROJECT: Thallium-201 Chloride for Diagnosis of Myocardial Ischemia and/or Myocardial Infarct

INVESTIGATORS: Principal: Robert Lull, LTC, MC

Associates: David L. Yuille, MAJ, MC
George Dunson, MAJ, MC
Brent Kehn, LTC, MC
Herbert Henry, MAJ, MC
Robert Telepak, MAJ, MC

OBJECTIVE: To evaluate the clinical utility of Thallium-201 for the detection of myocardial ischemia and/or myocardial infarction.

TECHNICAL APPROACH: The patient population to be studied includes active duty, retired, or dependent persons who are suspected of having ischemia heart disease or an acute or old myocardial infarction. Patients studied for myocardial infarction will be injected at rest, with 2-5mCi of Thallium-201 Chloride. Imagin of the heart will be performed in the anterior, LAO, and L. Latern positions. Persons suspected of having myocardial ischemia will be injected at the end of exercise during a standard Fredwill Stress EKG test. Imaging will be performed as above. Individuals having an abnormal exercise myocardial Image will then be restudied with a resting injection of Thallium-201. Results will be compared with clinical course, EKG and laboratory findings, and coronary arteriography where available.

PROGRESS & RESULTS: Approval for use of Thallium-201 was just recently granted. The first clinical use of Thallium-201 is expected shortly.

FUND: None.

FACILITIES TO BE USED: Nuclear Medicine Clinic LAMC

WORK UNIT NO. 400

TITLE OF PROJECT: Techniques of Vitreous Surgery I: Removal of Intravitreal Hemorrhage

INVESTIGATORS: Principal: Floyd L. Wergeland, Jr., COL , MC

Associate: Leon B. Metz, Jr., LTC, MC
Howard Cohen, LTC, MC

OBJECTIVE: To determine the best method and time for operating on an eye with traumatic vitreous hemorrhage in order to replace the vitreous with a physiologic salt solution and prevent the sequelae of vitreous organization and contraction leading to hopeless retinal detachments.

TECHNICAL APPROACH: There has been very little activity on this project. The responsible investigator has been transferred to Brooke Army Medical Center. However, COL Wergeland, who is the new responsible investigator has expressed his desire to continue the project. The project will be expanded to include the removal of traumatic ruptured lenses and retained intraocular foreign bodies, retinal detachment and double global perforations in the face of a vitreous hemorrhage. These problems are extremely important in the overall management of removal of vitreous in that they contribute greatly to the inflammatory and fibroplastic changes that occur following a traumatic injury.

WORK UNIT NO. 403

TITLE OF PROJECT: Ultrasonic Phako-Fragmentation and Irrigation of Cataracts

INVESTIGATORS: Principal: John Shock, LTC, MC

Associate: None.

OBJECTIVE: There have been very little activity on this project. The responsible investigator has been transferred to Brooke Army Medical Center. No other investigator is interested in continuing the project, therefore the study has been discontinued.

WORK UNIT NO. 405

TITLE OF PROJECT: A Cooperative Protocol for Prolonged Therapy of Mammary Cancer with L-phenylalanine Mustard as an Adjuvant to Surgery

INVESTIGATORS: Principal: Eugene P. Flannery, LTC, MC

Associate: Glen Justice, MAJ, MC

OBJECTIVE: This cooperative study is completed. Five LAMC patients have been studied under this project. Preliminary results published: NEJM 292: 117-122, 1975.

WORK UNIT NO. 406

TITLE OF PROJECT: Dynamic Rehabilitation of the Injured Knee: A New Concept

INVESTIGATORS: Principal: John A. Feagin, LTC, MC

Associates: Alan Freeland, MAJ, MC
Stephen Yamamoto, CPT, AMSC

OBJECTIVE: To develop newer techniques of rehabilitation of injured and postoperative knees. Disseminate information to other military installations regarding the above. To study gait abnormalities related to the injured and unstable knee. To develop newer methods for treatment of the injured and unstable knee.

TECHNICAL APPROACH: Three essential determinations are unobtainable by standard testing and physical examination: (1) objective reproducible measure of function; (2) objective measure of stability; and (3) a direct visualization of the interior of the knee. The equipment required is a standard gymnasium testing equipment already available at the Letterman Army Medical Center Gymnasium portable videotape unit to analyze pre and post operative function and an arthoscope to document the intraarticular pathology.

PROGRESS & RESULTS: The project is ongoing and that patients are treated each morning according to newer concepts at the Letterman Gymnasium. This is accomplished under the supervision of the Physical Therapy Department. MEDDAC Orthopaedic Service, Ft Ord, has been oriented and will participate in this research project. Gait Laboratory studies are on a continuing basis at the Shrine Hospital, San Francisco. Experimental ligamentous replacement will be undertaken on dogs with the Letterman Army Institute of Research.

FACILITIES TO BE USED: LAMC Gymnasium; Shrine Hospital, SF and LAIR Laboratory.

FUND: $190.00

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 407

TITLE OF PROJECT: Bowel Anastomosis Study

INVESTIGATORS: Principal: Paul T. McDonald, MAJ, MC

Associates: Harvey B. Conklin, COL, MC

OBJECTIVE: Controlled randomized prospective study of prepared colon anastomosis utilizing two accepted varied techniques, i.e., single vs double layer anastomosis and two types of suture, i.e., silk vs Ticron in order to determine which, if any, technique yields the least morbidity and mortality.

TECHNICAL APPROACH: All elective prepared general surgery patients who undergo colon anastomosis participated in the study. Evaluation of patients pre- and-post-operatively is routine, except informed consent was obtained for a contrast enema performed between postoperative day 10 and 14. Colon anastomosis was performed in one of four ways (single layer, Ticron; double layer, Ticron; single layer, silk; double layer, silk) on a completely randomized basis. Preoperative Evaluation: CBC with differential, urinalysis, electrocardiograms, chest x-ray, proctoscopic examination and barium enema. Preoperative bowel preparation: A standard mechanical and oral neomycin bowel preparation. No systemic antibiotics are used until an indication is noted in the postoperative period.

PROGRESS & RESULTS: 63 patients were entered in the study. Approximately 60 patients, i.e., those who did not give informed consent, who had systemic antibiotics,who had urgent or emergency surgery rather than elective surgery, did not complete a bowel preparation, or who had a protective colostomy or ileostomy did not qualify for the study. 14 patients with confirmed contrast enema leak had at least two days of fever temperatures greater than 100.5°F during the immediate postoperative period. One patient, #49 SS, had no fever and a very small radiographic leak. Total 15 patients. 20 patients with no barium enema leak had two days or more of fever greater than 100.5°F postoperatively, and 15 of these patients had documented reason for fever, i.e., atelectasis, urinary tract infections, or wound infection. 28 patients had no fever and no leak. Of 15 patients with confirmed contrast study leak, two required operation but 13 did not. These patients were managed by: ignoring the leak if it was small and the patient was afebrile with normal bowel function; giving the patient prolonged clear liquid diet if bowel function was delayed, ie., greater than seven days postoperatively; for large leak treatment with IV antibiotics and nasogastric suction until good bowel function returned. Two large leaks on nasogastric suction, IV fluids and antibiotics required re-operation and colostomy. Project completed.

FACILITIES TO BE USED: General Surgery Clinic LAMC

FUND: None required.

TITLE OF PROJECT: Bowel Anastomosis Study

PUBLICATION & CONCLUSIONS: The study did not have adequate patients to prove the superiority of any of the four type anastomoses. Gentle contrast enema during the period 10-14 days after surgery is a safe technique for study of colon anastomosis. No complications could be attributed to the study. Low anterior resection leak rate is approximately 50% (9 of 20) as suggested by Goligher's work. Left colon(sigmoid) lead rate is less, ie., 4 of 21, and transverse colon is least, 2 of 22. Patients who have no postoperative fever and rapid return of bowel function do not have significant leaks (only one small leak noted in afebrile patients). Patients with fever or prolonged return of bowel function have a high incidence of demonstrable leaks, however, most may be managed conservatively and do not require surgical intervention (only 2 of 15). Colonic bowel anastomosis may be performed with either one or two layer silk or Ticron sutures with good results. However, in low anterior anastomosis, the double layer silk had the highest leak rate.

WORK UNIT NO. 410

TITLE OF PROJECT: Chloroquine Distribution in the Eye

INVESTIGATORS: Principal: Bradley C. Black, CPT, MC

Horace B. Gardner, LTC, MC

OBJECTIVE: To determine distribution of C-14 labelled chloroquine in the pigmented rabbit eye.

TECHNICAL APPROACH: Project is completed. Paper has been presented at two local conferences(LAMC Ophthalmology and Department of Surgery LAIR). Final report will follow.

FUND: None.

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 411

TITLE OF PROJECT: The Effect of Intravenous Lorazepam (WY-4036) on the Resting Ventilation and Ventilatory Response to Carbon Dioxide in Man

INVESTIGATORS: Principal: Bradford A. Paulson, MAJ, MC

Associates: James Salerno, MAJ, MC
Terry Vitel, MD
Walter Way, MD

OBJECTIVE: To determine if intravenous Lorazepam causes respiratory depression or enhances the respiratory depression caused by meperidine when used as a preoperative medication.

TECHNICAL APPROACH: This study is completed. 27 healthy patients scheduled for elective surgery were studied in the immediate preoperative period. Patients received one of the following drugs intravenously on the morning of surgery: (1) Lorazepam 3.5 mg/70kg (2) Lorazepam 3.5 mg/70kg plus meperidine 50 mg/70kg (3) Lorazepam 3.5 mg/70kg plus meperidine 100 mg/70kg (4) Meperidine 100 mg/70kg. Measurements of ventilatory response to CO_2 were performed 15, 30, 60 and 120 minutes after injection. These post injection measurements were compared with a single measurement of ventilatory response to CO_2 obtained prior to injection of the drug. After the final measurement at 120 minutes was obtained the patients were taken to the operating room for their surgery. To facilitate analysis of the data, five patients from each drug regimen were randomly selected. The data for the 20 patients (4 drug groups) was then analyzed by 2 way analysis of variance with replication. The results indicated that Lorazepam did not produce respiratory depression nor enhance the respiratory depression caused by Meperidine. These results were statistically significant with a P of $<.055$.

FUND: $217.00

PUBLICATION & CONCLUSIONS: A paper is being prepared and will be submitted for publication.

WORK UNIT NO. 412

TITLE OF PROJECT: Comparison of Arterial Blood Gases in Post-Operative Cesarean Section Patients vs Routine Post Vaginal Delivery Patients

INVESTIGATORS: Principal: Craig A. Winkel, MAJ, MC

Associates: John B. Schlaerth, MAJ, MC
Donald L. Snyder, COL, MC

OBJECTIVE: This study was not be pursued by the primary investigator. The principal reason was availability of time by the investigator. No other resident is interested in the project, therefore it has been removed from the files.

WORK UNIT NO. #413

TITLE OF PROJECT: Comparison of Perineural vs Epineural Nerve Repair in Cats and Monkeys

INVESTIGATORS: Principal: H. Edward Cabaud, MAJ, MC

Associates: Sterling B. Mutz, COL, MC
John J. Niebauer, MD

OBJECTIVE: The purpose of this study was to compare the results of intrafasicular perineural and epineural neurorrphaphies in the same experimental animal so that each animal would serve as his own control.

TECHNICAL APPROACH: 20 mongrel house cats underwent acute lacerations and neurorrhaphies of both ulnar nerves above the medial epicondyle. One nerve was repaired using the standard epinerual techniques with 8-0 nylon. The other nerve was repaired using a intrafasicular perineural technique with 10-0 nylon at 10-16 power magnification. The cats were allowed unrestricted activities for a period of 4 to 5 months and then were evaluated for return of function. Subjective evlauation included gait observation, fanning of claws, and withdrawal from pin-prick. Objective evaluations included efficiency and absolute strength of the flexor carpi ulnaris muscle, individual weight of the flexor carpi ulnaris muscle and actual axon counts proximal and distal to the anastomosis site - a total of 80 individual axon counts. This objective data was subjected to statistical analysis to compare the results of intrafasicular perineural and epineural neurorrhaphies. Histologic studies of the neuromas and flexor carpi ulnaris muscles were also included in the evaluation. An extremely satisfactory experimental model has been developed to compare the results of different types of nerve repairs. The results of this study provide invaluable information in determining the efficacy of intrafasicular perineural neurorrhaphy as compared to epineural neurorrhaphy. This study is completed.

FUND: $1,477.24

PUBLICATION & CONCLUSIONS: Paper submitted for publication.

WORK UNIT NO. 414

TITLE OF PROJECT: A Simple, Inexpensive Technique for Intraoperative Coronary Angiography

INVESTIGATORS: Principal: Maurice E. Lindell, COL, MC

Associate: None.

OBJECTIVE: To determine usefulness, feasibility and hazards of a simplified technique for intraoperative coronary angiography, and if feasible, to develop the technique for efficient clinical use.

TECHNICAL APPROACH: With the animal on cardiopulmonary bypass and induced ventricular fibrillation, a 23 ga scalp vein needle is introduced into the coronary artery at the site selected for arteriotomy, or in the case of a completed graft, into the vein graft wall. Several cc's of angiographic contrast material are hand injected and a portable xray used, sterile (kidney) film placed behind the heart in the pericardium. Xrays will be evaluated for clinical usefulness, techniques applicable to human use will be developed, and dog hearts will be examined for adverse effects.

PROGRESS & RESULTS: Dogs were anesthetized and placed on Cardiopulmonary Bypass. Ventricular fibrillation was induced. A 23 guage scalp vein needle was intorduced into the coronary artery to be studied and several cc of angiographic contrast material hand injected. A portable x-ray machine was used with exposure on flexible, sterile(kidney) film placed behind the heart. Technique and exposure factors were standardized so that satisfactory angiograms could be consistently obtained. Though not recommended by the manufacturer, gas sterilization of the film was found to be effective without significant film damage. All dogs were removed from Cardiopulmonary bypass and were able to sustain adequate circulation. Preserved dog hearts are now being examined to determine if there is coronary artery damage due to the needle or the hematoma that follows its removal.

FACILITIES TO BE USED: Laboratory at LAIR.

FUND: None.

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 415

TITLE OF PROJECT: Repair and Management of Penetrating Trauma to the Kidney

INVESTIGATORS: Principal: LTC Jack W. McAninch, MC

Associates: CPT William Rodkey, DVM, VC
COL Ray E. Stutzman, MC
MAJ Lloyd J. Peterson, MC

OBJECTIVE: To develop an animal model to study missile injury to the kidney under controlled conditions. Subsequently, different methods of treatment could be compared in order to determine the most effective method of preserving renal tissue.

TECHNICAL APPROACH: Mongrel dogs weighing approximately 40kg were used for the study. A spring-loaded traumatizing device was developed and proved to be most effective in delivering a consistent penetrating injury to the kidney. The kidney was exposed through a transabdominal approach and the spring-loaded device used to deliver a penetrating injury to the lower aspect of the left kidney. After appropriate management of the injury a right nephrectomy was done in all cases. The injuries were managed by two methods. In one group a partial nephrectomy was done in-situ with the renal artery clamped during the repair. The partial nephrectomy was done by excising all damaged tissue followed by individual suture ligation of bleeding points. The capsule was then approximated over the surgical defect. Management of the second group of animals consisted of complete transection of the renal artery and vein with the kidney being placed on an operative bench were extracorporeal partial nephrectomy was performed. The ureter was left intact in all cases. Continuous perfusion with Sack's solution at 4° C was instituted while the partial nephrectomy was being done and the remaining repair completed. The kidney was then autotransplanted to the left iliac fossa using an end-to-side anastomosis of the renal vein to the common iliac vein and end-toend anastomosis of the external iliac artery to the renal artery. All animals received 12 grams of Mannitol prior to inflicting the renal injury and an additional 12 grams of Mannitol was given at the completion of the procedure. The animals received antibiotic therapy for five days following operation. Serum creatinine values were monitored preoperatively and on a daily basis for the first seven post-operative days. Additional studies were drawn at 14 and 21 days. 21 days postoperatively the animals had aortography performed to evaluate the arterial anastomosis, renal size and vascular patterns. Necropsy was then performed.

TITLE OF PROJECT: Repair and Management of Penetrating Trauma to the Kidney

PROGRESS & RESULTS: 8 animals were included in Group I using the in-situ partial nephrectomy technique. One animal in this group died. The pre-operative average creatinine was 1.1 mg% with values of 2.3, 2.7 and 2.4 noted on the first three postoperative days. The value was noted to drop to 1.9 at seven and 14 days postoperatively. The average ischemia time for this group of animals was 19 minutes. Aortography was normal in six animals and showed a poor nephrogram in one. Necropsy demonstrated significant fibrotic changes in the renal fossa area in two kidneys. Group II had eight consecutive animals done with lower pole injury using the extracorporeal technique and autotransplantation. One animal was lost secondary to arterial thrombosis. The average preoperative creatinine for these animals was 1.1 mg% with 2.7, 2.6 and 2.4 mg% noted on the first three postoperative days. The seventh postoperative day value was 2.9 and at 14 days 2.2 mg% and on the 21st postoperative day 1.8 mg% creatinine value was present. The total ischemia time for this procedure averaged 72 minutes, and during this time an average of 19 minutes for cool perfusion was done. The aortogram was considered normal in all cases. Necropsy was considered normal and shows no evidence of unusual fibrosis or scarring.

PUBLICATION & CONCLUSIONS: Additional studies are being done at the present time comparing extracorporeal repair and autotransplantation with in-situ repair of injuries to the midportion of the kidney. Two scientific publications expected to come from this protocol based on the present study are: (1) "A mechanical device for standardization of renal injury." (2) "Experimental penetrating renal trauma: A comparison of bench and in-situ repair."

FACILITIES TO BE USED: Comparative Medicine Department LAIR.

FUND: Animals $2,278.17

WORK UNIT NO. 417

TITLE OF PROJECT: The Effect of Intravenous Droperidol on the Resting Ventilation and Ventilatory Response to Carbon Dioxide in Man

INVESTIGATORS: Principal: Bradford A. Paulson, MAJ, MC

Associates: James A. Meyer, COL, MC
Lawrence D. Becker, MD, Univ of Calif, SF
Walter L. Way, MD, Associate Professor, Univ Of Calif, SF
Ronald D. Miller, MD, Univ of Calif, SF

OBJECTIVE: To determine if intravenous Droperidol causes respiratory depression when used as a preoperative medication.

TECHNICAL APPROACH: This study is completed. 20 healthy patients scheduled for elective surgery were studied in the immediate preoperative period. Patients received one of the following drugs intravenously on the morning of surgery: (1) Droperidol: a. 0.075 mg/kg. b. 0.15 mg/kg. c. 0.30 mg/kg. (2) Placebo-diluent volume: Measurements of ventilatory response to CO_2 were performed 15, 30, 60 and 120 minutes after injection. These post injection measurements were compared with a single measurement of ventilatory response to CO_2 obtained prior to injection of the drug. After the final measurement at 120 minutes was obtained, the patients were taken to the operating room for their surgery. The data for the 20 patients (3 drug groups and placebo group) was analyzed by two way analysis of variance with replication. Results indicate that Intravenous Droperidol produces marked respiratory stimulation when given intravenously. This stimulation was observed especially in the groups receiving 0.15 and 0.30 mg/kg of Droperidol. These changes were significant with a P value <0.005.

FUND: None.

PUBLICATION & CONCLUSIONS: A paper is being prepared and will be submitted for publication.

WORK UNIT NO. 418

TITLE OF PROJECT: The Cardiac Hemodynamic Changes Associated with Clamping and Unclamping of the Infrarenal Abdominal Aorta in Patients with and without Ischemic Heart Disease

INVESTIGATORS: Principal: Frederick A. Campos, MAJ, MC

Associates: Robert G. Hajny, MAJ, MC
Stephen C. Sitter, LTC, MC
Barbara Holland, CPT, AN
Paul T. McDonald, MAJ, MC
John H. Hutton, LTC, MC
Terry Clemmer, LTC, MC

OBJECTIVE: To determine the hemodynamic changes which occur during the induction of anesthesia with H_2O and halothane, and endotracheal intubation. To determine whether prior heart disease effects induction of anesthesia and endotracheal intubation. To determine effect of infrarenal abdominal aorta cross-clamping on cardiac hemodynamics and whether there is a difference in patients with and without heart disease.

TECHNICAL APPROACH: Patients admitted to LAMC for elective aorto-femoral bypass or for resection of an infrarenal abdominal aortic aneurysm will be the candidates of this study. Routine peri-operative monitoring of such patients presently includes the insertion of arterial and central venous catheters. Swan-Ganz catheters rather than CVP lines are utilized in those patients in whom it is felt that right-sided heart pressures might not accurately reflect "left heart" hemodynamics. Routine pre-operative evaluation will include history and physical examination, especially with reference to coronary artery disease, chronic pulmonary disease, renal disease and hypertension. Laboratory evaluation will include CBC, urinalysis, SMA 6 and 12, PT, PTT, platelet count, chest xray, electrocardiogram, and simple spirometry pulmonary function tests. The patients would sign informed consent as to his or her inclusion and awareness of the nature of the study; including insertion of a Swan-Ganz and arterial catheters, and for their peri-operative use for hemodynamic and pulmonary monitoring and blood sampling. The patients will be divided into two groups: (1) No evidence of ischemic heart disease (2) Evidence of ischemic heart disease as manifested by prior myocardial infarction, a history of angina pectoris or electrocardiographic evidence of ischemia or infarction.

PROGRESS & RESULTS: Project is tentatively completed pending statical analysis of data. 17 patients have been studied. 7 patients were evaluated with controlled halothane concentration during cross-clamping and 10 patients with controlled anesthetic induction. Approximately half of the patients in each group have evidence of heart disease. Preliminary data analysis indicates that anesthetic induction itself results in cardiac hemodynamic changes which differ from the effects of endotracheal intubation. The changes

TITLE OF PROJECT: The Cardiac Hemodynamic Changes Associated with Clamping and Unclamping of the Infrarenal Abdominal Aorta in Patients with and without Ischemic Heart Disease

which occur with cross-clamping do not appear to differ in patients with or without heart disease. Full results of this project will be submitted to a major anesthesiology journal for publication.

FUND: Consumable $222.48 MEDCASE None

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 419

TITLE OF PROJECT: Effects of Phacofragmentation and Irrigation on Rabbit corneal Endothelium

INVESTIGATORS: Principal: Joseph B. Barron, MAJ, MC

Associate: Steven Schuschereba, Biological Assistant

OBJECTIVE: To observe the effects of the technique of ultrasound and irrigation on the rabbit corneal endothelium.

TECHNICAL APPROACH: Young adult albino rabbits weighing between 2-3kg, with no known ocular abnormalities were randomly divided into groups, usually with five corneas in each group. The animals were anesthetized with 2% surital after a preinjection of acepromazine. The pupils were dilated with 15% neosynephrine and 1% cyclocyl and a wire speculum was placed for lid retraction. With aid of the operating microscope a limbal incision of 3-4 mm was made into the anterior chamber with a #11 scalpel blade in any convenient superior location. Control Group - 5 corneas: This group served as the control group. After the anterior chamber was entered with the #11 scalpel blade the corneas were stained, removed, and photographed to evaluate corneal endothelial damage. Evaluation of Irrigation: In these eyes, the needle from the phacofragmentor was introduced into the anterior chamber and the tip placed centrally in the visual axis. Lactated Ringer's solution was irrigated through the needle at a slow drip. Care was taken not to traumatize the corneal endothelium or lens. No ultrasound was used. The corneas were stained, removed, and evaluated for endothelial damage.

PROGRESS & RESULTS: Project is completed. Photomicrographs of the endothelium stained with trypan blue revealed a good endothelial mosaic in all five corneas. There was no stain uptake in two, uptake by less than 5% of the cells in two and less than 25% uptake in one cornea. Electron microscopy showed some surface irregularity in one cornea and deposits of fibrin were found. Holes were occasionally found at the junction site between three cells. Lactated Ringer's--Gross and photomicroscopic examination of corneal endothelium was no different from control eyes except that one cornea showed death of some of the endothelial cells with diffusion of the stain diffusely beneath the endothelium. Further progress of cell damage was found in scanning electron microsurgery as vacuolation of cellular membranes was noted in a few areas. Lactated Ringer's with epinephrine--Gross analysis with trypan blue were similar to control corneas. There was a general increase in the number of staining cells on photomicroscopy as compared to controls on those corneas after irrigation with lactated Ringer's with all five corneas showing some staining, at least in focal areas. Electron microscopy showed an increase in surface irregularity and an increase in endothelial cell destruction in focal areas from the control or irrigation with lactated Ringer's only groups. Electron photomicrographs of the endothelial cells have been analyzed statistically to determine quantitative effects of manipulation on endothelial cell damage.

TITLE OF PROJECT: Effects of Phacofragmentation and Irrigation on Rabbit Corneal Endothelium

FUND: Consumables $49.50 Animals $891.47

PUBLICATION & CONCLUSIONS: Rabbit corneas are thin and difficult to handle without producing some endothelial damage. Trypan blue staining is a sensitive method of detecting damage to cellular membranes. Slight amounts of increased endothelial damage as evidenced by an increased number of corneas taking up the trypan blue in photomicrographs and an increase in vacuolation of the endothelial cells were noted when epinephrine was added to lactated Ringer's irrigating solution. There was also a slight increase in damage when comparing those corneas irrigated with lactated Ringer's over control eyes. The scattered areas of endothelial damage produced with the ultrasound needle in the lens only or in the technique of phacofragmentation may be due in part to the ultrasound, but other mechanical factors such as the collapse of the anterior chamber and the contact between the endothelium and lens certainly contributes wholly or in part to this damage. Endothelial damage is obviously produced by the vibrating needle tip when it is held stationary in the anterior chamber. Care should be taken to have this tip in lens material when the machine is in operation.

AWARD: Major Kenyon Joyce Award.

WORK UNIT NO. 420

TITLE OF PROJECT: The Fate of an Autogenously Transplanted Artery in the Growing Dog

INVESTIGATORS: Principal: John E. Hutton, Jr., MC, COL

Associates: Barry Gardiner, MAJ, MC
Norman M. Rich, COL, MC
Edwin J. Wylie, MD

OBJECTIVE: To demonstrate the fate of an autogenously transplanted artery or vein in a growing animal; will it continue to exhibit its potential for growth (length, diameter, elasticity) once removed from its original location.

TECHNICAL APPROACH: The experimental model will be the dog, specifically a puppy, age two months of large parentage (German Shepard, etc). It is assumed that a two month old puppy is comparable in growth potential to a five year old human, and that the puppy is fully matured at ten months of age. The animals will be grouped into three categories according to the procedures performed. (1) two dogs in which the external iliac arteries will be divided on one side and subjected to an end-to-end interrupted anastomosis with 6 or 7-0 vascular suture. This will serve as a control, i.e., will the anastomosis grow in diameter or might this be the limiting factor to an arterial repair; (2) two dogs will undergo resection of a 2cm length of the external iliac artery, and then re-insertion of this segment into its original site (two vascular anastomoses). On the contralateral side, a similar segment will undergo careful dissection of the periadventitial tissues for a length of 2cm. The vessel will then be left in place. The latter procedure will serve as the control demonstrating the effects of dissection of the periadventitial tissue from the vessel walls without actual division of the vessel; (3) two dogs will undergo resection of 2cm segments of both external iliac arteries, and these will be exchanged and re-inserted into the arterial system, thereby evaluating the growth potential of the excised and transplanted artery.

PROGRESS & RESULTS: The study has progressed well. Four dogs were entered into the test group when at a weight of five to six pounds and at an age of about two months. The first dog had a simple division of the femoral artery bilaterally and the cut ends re-anastomosed with interrupted 8-0 Tevdek sutures. Immediate operative arteriograms showed no defects at the anastomtic sites (the areas of anastomosis could not be determined by inspection of the arteriogram). With the technique of anastomosis established, the subsequent three puppys underwent dissection of the artery only on the right side, and resection and re-insertion of an arterial segment on the left side, again using interrupted sutures of 8-0 Tevdek for the anastomosis. The first three dogs have undergone operative arteriography at full maturity (12 months of age, 50-55 lbs.), again demonstrating no defects or stenosis at any of the

TITLE OF PROJECT: The Fate of an Autogenously Transplanted Artery in the Growing Dog

suture lines, and no interruption of growth in the divided and re-inserted segment. The first three dogs have been sacrificed and the arterial segments in question inspected, photographed, and submitted for histological preparation.

Our impression is that: (1) with good technique, immature arteries may be anastomosed in an end to end fashion without stenosis as the diameter of the vessels increases with maturity, and (2) that an immature artery of similar caliber will probably maintain its growth potential if used as a graft.

With the excellent results obtained at this point, the next phase should include (1) transplanting an artery of suitable caliber but from another area, specifically inserting a segment of the internal iliac artery into the femoral artery. This should require two dogs. We have been unable to find a suitable vein for such trial implanation in the dog.

FACILITIES TO BE USED: LAIR Laboratory.

FUND: Consumables: $109.00 Animals: $5,107.76

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 421

TITLE OF PROJECT: Experimental Spinal Cord Trauma: Comparison of Empirical Treatments

INVESTIGATORS: Principal: William G. Rodkey, DVM, CPT, VC

Associate: David G. Fairchild, MAJ, MC
Lynn S. Hedeman, MAJ, MC

OBJECTIVE: This study compares various empirical treatments and will describe a clinically applicable mode of therapy to be employed in spinal cord injuries. Because no adequate therapy exists for effective treatment of acute spinal cord injuries, basic information derived from this study will be very useful to both military and civilian physicians.

TECHNICAL APPROACH: A T-10 laminectomy will be performed on mongrel dogs weighing 15 to 20 kg. Each animal will receive a 500 gm-cm force to its spinal cord using the standard technique. A small anvil will be placed over the cord and will be struck by a weight dropped through a cylindrical tube from a measured height. The weight multiplied by the distance will equal 500gm-cm. A myelotomy will be done 2 hours post-trauma, and intrathecal administration of medications will begin immediately following the myelotomy. For animals receiving pressors or depressors, the intravenous administration will commence 15 minutes post-trauma and continue for 4 hours. Through the entire surgical procedure the arterial blood pressure will be monitored at the level of the heart. A venous catheter will be maintained in all animals and IV fluids will be administered as needed post-operatively. Group I - 5 dogs, control (trauma but no therapy). Group II - 5 dogs, myelotomy plus intrathecal placebo(isotonic saline). Group III - 5 dogs myelotomy plus intrathecal phenoxybenzamine(5-10ml) 10-4M. Group IV - 5 dogs myelotomy plus intrathecal cyproheptadine(5-10ml) 10-4M. Group V - 5 dogs, myelotomy plus IV mitroprusside to depress mean arterial pressure by 30mmHg. Group VI - 5 dogs, myelotomy plus IV levophed to increase mean arterial pressure by 30mmHg. Group VII - 5 dogs, myelotomy plus parenteral corticosteroids(Solu-Medrol).

PROGRESS & RESULTS: This project is, in essence, completed. All surgical procedures have been performed and only one dog remains to be studied. All other animals have been photographed, and their spinal cords have been examined histologically. Upon termination of the final dog, all motion pictures of the animals will be reviewed and graded by unbiased observers. Likewise, the histologic sections will be graded for degree of necrosis by unbiased observers. The clinical and histologic interpretations will be compared.

FUND: Animals $7,164.00

PUBLICATION & CONCLUSIONS: Spinal cord trauma in dogs was treated empirically

TITLE OF PROJECT: Experimental Spinal Cord Trauma: Comparison of Empirical treatments

by one of the following: a. Intrathecal saline. b. Intrathecal phenoxybenzamine. c. Intrathecal cyproheptadine. d. Intrathecal saline plus IV mitroprusside. e. Intrathecal saline plus IV levophed and f. intrathecal saline plus parenteral corticosteroids (Solu-Medrol). Clinical recovery is being compared to the histologic appearance of the cords 21 days after trauma. Although the treatment code has not been revealed, it appears that the cyproheptadine group had the best clinical recovery. If statistical analysis supports this, the information will indeed prove highly useful. The introduction and methods sections are currently in draft. As soon as all final evaluations are completed, the remainder of the paper will be prepared. A draft of the paper should be ready within 6-8 weeks. The final paper will be submitted to the Journal of Neurosurgery.

WORK UNIT NO. 423

TITLE OF PROJECT: Constant Pressure Goldman Tonometry

INVESTIGATORS: Principal: Lewis Lauring, LTC, MC

Associate: LTC Horace Gardner, MC

OBJECTIVE: To clinically evaluate a simplified method of Goldman Tonometry

TECHNICAL APPROACH: Utilizing a measuring eye piece in the Haag-Streit slit lamp, the exact under or over area of applanation can be noted. During routine Goldman applanation tonometry, the tonometer will be set at a fixed level and the cornea applanated. The amount of over or under applanation will then be noted and the applanation pressure adjusted in the usual Goldman applanation method. The actual pressure as recorded by conventional Goldman applanation tonometry will then be recorded. The correlation between the theoretical applanation area curve and the actual measurement obtained from patients, plus a clinical evaluation of the ease and time required for this method will be analyzed.

PROGRESS & RESULTS: Using the Haag-Streit measuring eye piece to estimate the under or overlap area of applanation, we have found that there was a good correlation between measured and observed(estimated) intraocular pressure. The eye piece however was impractical because of poor visibility and the necessity to constantly change eye pieces. The next stage in the project is to score the plastic tip of the Goldman applanation with a lined grid and use this since the optics will be better as well as the illumination. Because of the departure of both investigators, Doctor R. Hector, Ophthalmology Service will be continuing this project.

FUND: $504.80.

FACILITIES TO USED: Ophthalmology Clinic

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 426

TITLE OF PROJECT: The Evaluation of the Optical Sciences Group(OSG)Prototype Instrument for Objective and Automated Measurement of Visual Acuity Army Contract *DAMD 17-75-C-5055*

INVESTIGATORS: Principal: Anthony J. Adams, O.D., Phd

Associates: Horace Gardner, LTC, MC
Floyd Wergeland, COL, MC
David Johnson, LTC, MC
Merton C. Flom, O.D., Phd
Arthur Jampolsky, MD

OBJECTIVE: Phase III of this study is designed to evaluate the OSG acuity test for malingerers and unusual visual conditions which can be expected in the Army population (amblyopia, high astigmatic errors). This phase should precede any phases designed to validate the devise by technicians.

TECHNICAL APPROACH: Phase II of the project is completed. 69 patients were studied. Data has been collected and final report will be forwarded to TSG by Dr. Anthony J. Adams. Phase III is planned to be operational at LAMC by the 28th of July 1976.

FACILITIES TO BE USED: Optometry Clinic LAMC.

FUND: Budget has been approved by R&D for Phase III.

Personnel:	$8452.00
Services	1450.00
Consumable supplies	575.00
G&A (20%)	2210.00
Fee (8%)	1061.00
Total	$14323.00

PUBLICATION & CONCLUSIONS: None

WORK UNIT NO. 427

TITLE OF PROJECT: The Endoscopic Effects of Laser on the Lower Urinary Tract of Canines

INVESTIGATORS: Principal: Lloyd J. Peterson, MAJ, MC

Associates: Ray E. Stutzman, COL, MC
Jack W. McAninch, LTC, MC
Edwin S. Beatrice, LTC, MC
Bruce E. Stuck, Research Physicist
David J. Lund, Research Physicist
William Rodkey, DVM, CPT, VC

OBJECTIVE: This pilot project has the purpose of determining the effect of laser radiation delivered endoscopically via a fiberoptic system to the lower urinary tract of dogs. The amount and preciseness of tissue destruction and the subsequent healing process is the information being sought in this initial endeavor. This information will allow us to ascertain biologic safety levels and consider medical applications on a therapeutic level.

TECHNICAL APPROACH: Initial phases of research will begin with the endoscopic fulguration of the bladder of 12 female dogs in four different areas of the bladder. Each area will receive a different intensity of radiation and exposure time, but corresponding areas in each animal will be the same. The laser unit has built in settings to control both intensity and exact time of exposure. Necropsy will be performed on two animals at each of six postoperative periods (30 minutes, 24 hours, 3 days, 1 week, 2 weeks and 4 weeks). Gross and microscopic exam will allow us to determine the depth, extent and accuracy of tissue damage. The healing stages will also be evaluated at the same time. Six dogs will undergo fulgruation of one urethral orifice and follow-up IVP's obtained at 1 week. Three dogs will be necropsied then and the other three dogs will have IVP's and necropsy performed at 4 weeks postoperative. Four dogs will undergo endoscopic incision of the urethral sphincter and evaluated postoperative for development of incontinence. Necropsy of two dogs at 1 week and two dogs at 4 weeks will be carried out for pathological exam. After completion of these initial studies, creation of experimental lesions in dogs will be developed for trials of therapy with the laser. Hemorrhage from cold blade incisions in the bladder and tumor from chemical carcinogens would be the most likely courses to follow. The hemorrhagic lesion would determine feasibility to treat bleeding from trauma to the bladder.

PROGRESS & RESULTS: Initially, spectrophotometry of four canine bladders was accomplished through the range of water transparency in order to measure transmission and reflectance and consequently to determine an absorptive curve through these wavelengths. Absorptive peaks were located near the principal argon wavelengths of 4880 and 5145 Angstroms. Other impressive absorptive peaks were in wave lengths without appropriate or practical laser

TITLE OF PROJECT: The Endoscopic Effects of Laser on the Lower Urinary Tract of Canines

delivery systems (this information has already been submitted for publication). The argon laser was then applied to dog bladders in a basin of water to simulate endoscopic conditions. Using appropriate eye protection with argon safety goggles, several lesions were created in this ex-vivo situation. An initial series of eight dogs then underwent endoscopic application of the laser through a fiberoptic light bundle within a #7 French urethral catheter. This was delivered through standard cystoscopic equipment to the dog bladder both through the urethra and through suprapubic cystostomies. It was noted that lesions were produced with the apparatus running at maximum power output applied over time periods of 5-20 seconds. Initial pathology showed coagulation and destruction of mucosa and submucosa with some specimens showing superficial muscle coagulation. Two more animals were then subjected to application of the laser and discrete lesions again were made at 5, 10 and 20 seconds of exposure and it was noted that the measured output of the machine itself was 2.5 to 2.6 watts but after delivery through the fiberoptic cable system the power output at the tip of our illuminating cable dropped to 1.7 to 1.8 watts. These, as the previous animals, were immediately sacrificed and discrete circumferential shallow white superficial ulcers were noted in the gross specimen. Cystoscopic photography was completed at that time to document the technique and record the results seen immediately at cystoscopy. The project is now continuing with a series of survival experiments with the dogs being sacrificed at 24 hours, 3 days, 7 days, and 4 weeks after creation of the lesions in order to determine the subsequent healing and reparative processes.

FACILITIES TO BE USED: Laser Safety Research area at LAIR and the Comparative Medicine Department LAIR.

FUND: Animals $1,271.11. Rental $800.00

PUBLICATION & CONCLUSIONS: Paper submitted for publication.

WORK UNIT NO. 428

TITLE OF PROJECT: Superior Vena Cava Replacement with Gore-tex

INVESTIGATORS: Principal: William H. Heydorn, COL, MC

Associates: William G. Rodkey, CPT, VC
William Y. Moores, MAJ, MC

OBJECTIVE: To evaluate tubular grafts of Gore-tex(polytetrafluoroethylene) for replacement or bypass of the superior vena cava. Gore-tex is composed of teflon nodules which are interconnected by thin flexible fibrils. The pore size of the material can be varied so as to provide an open structure which allows rapid tissue ingrowth. Since there is no satisfactory prosthesis available for large vein replacement, this study will evaluate the material in general and more specifically the proper pore size.

TECHNICAL APPROACH: To replace or bypass the superior vena cava in 25 dogs. This will be done in 5 series. Series I will be a control in which the cava will be excised and then sewn back in place. Series II will consist of excision of the cava and replacement with a 5cm segment of five micron Gore-tex. Series III will consist of excision of the cava and replacement with spiral supported 30 micron Gore-tex. Series IV will consist of caval excision and replacement with 30 micron Gore-tex. Series V will consist of excision and replacement with 90 micron spiral support Gore-tex. Mongrel dogs weighing 15-30 kilograms will be anesthetized with endotrachial anesthesia. Caval replacement with Gore-tex tubes will be done(except control group). 6.0 prolene suture will be used. A proximal internal thoracic artery - caval shunt will be made with subsequent flow measurements. Chest tube will be left in place until dog is ready for extubation. A control group of five dogs and four groups with different types of Gore-tex grafts will be followed up to one year.

PROGRESS & RESULTS: 18 dogs have been operated upon. There have been four deaths, one in the initial 72 hours period. 14 dogs are being followed. The operative portion of the experiment will be completed in September or October. The entire experiment should be completed in April or May 1977. At this time, the material will be evaluated in terms or long term patency and pathological evaluation of the dogs response to the graft material. If the material should prove to be satisfactory, the type graft with the most promise will be further investigated in regard to using longer tubes in other locations.

FUND: $4,804.03

FACILITIES TO BE USED: Animal Laboratory LAIR.

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 429

TITLE OF PROJECT: Topical Steroid Therapy for Rhus Dermatitis

INVESTIGATORS: Principal: George L. McElroy III, CPT, MC

Associates: Joseph Greenberg, LTC, MC
Frank W. Crast, MAJ, MC
James L. Stewart, COL, MC

OBJECTIVE: To determine if any topical steroid agent was efficacious in the treatment of rhus contact dermatitis and to determine which is the most cost effective agent.

TECHNICAL APPROACH: Project terminated. The guinea pigs used were more difficult to sensitize to rhus then we had expected. We only were able to follow the natural course of rhus contact in the guinea pig and also we learned better ways of sensitizing to this antigen. No drug therapy trial was undertaken. A presentation of the histopathology of rhus contact is planned for the AFCR in Carmel California in February 1977.

WORK UNIT NO. 430

TITLE OF PROJECT: Computer-Controlled Ophthalmic Refraction, US Army Medical Research and Development Command Contract #DADA-17-72-C-2044

INVESTIGATORS: Principal: Elwin Marg, PhD, University of California Berkeley

Associates: David Johnson, LTC, MSC

OBJECTIVE: To use the computerized refractor system to perform certain visual tests. The primary goal is to perform a subjective eye refraction examination by computer.

TECHNICAL APPROACH: 50 volunteer patients from the Optometry Clinic will be examined with the aid of the computerized system in addition to their regular examination. The computer communicates with the patient by means of audio magnetic tape by which messages are selected by the program through the computer algorithms and by this means the patient is given the various commands and instructions. The following tests will be automatically performed: (1) Visual Acuity, unaided (2) Visual Acuity with old prescription (3) Refined Sequential Sphere (4) Radial Line Axis Determination (5) Crossed Cylinder Axis Determination (6) Crossed Cylinder Power Determination (7) Refined Sphere (8) Visual Acuity with Recommended Distance Prescription and (9) Near Tests. These tests are designed to give maximum convex or mimimum concave lens for maximum visual acuity. The refraction procedure involves seating the patient behind a computerized refractor. The examination probably will take between 15 and 30 minutes, but no more than an hour. Upon its completion the computer suggests a prescription for glasses which includes the spherical and cylindrical powers, and cylindrical axis. The visual acuity is determined through this recommended prescription. Comparisons will be made primarily on the basis of visual acuity from the prescription. Any differences will be analyzed.

PROGRESS & RESULTS: The Refractor III system, consisting of a computer-actuated refractor, Digital Equipment Corporation PDP-8/E computer, and ancillary equipment was moved from the University of California campus at Berkeley to the facility designed for it at the Optometry Clinic, LAMC. 57 patients were tested and their data analyzed. All patient-volunteers were handled in accordance with AR 40-38, and their consent was obtained on the approved form. Preliminary analysis of the initial data indicates that approximately 83% of the patients obtained a satisfactory prescription. 17% of the patients did not for the following reasons: 6+% were unsatisfactory because of an identifiable error, either in the flow charting or in the software or hardware. These errors are correctable and some of them have already been taken care of. 6+% were unsatisfactory because of unidentifiable causes. It is expected that these causes will be identifiable in the future and the next series of patient-volunteers will be examined carefully to this end. Once the cause is identified the patient can be put either into the previous grouping, i.e., unsatisfactory for identifiable reasons, or into the next grouping. This next and final grouping consists of those who make fundamental errors, that is, errors which are not dependent on the system per se.

TITLE OF PROJECT: Computer-Controlled Ophthalmic Refraction, US Army Medical Research and Development Command Contract #DADA-17-72-C-2044

This group, which consists of about 4% of the patients, seemed confused no matter clear and careful the instructions were. In this group are those who have physical handicaps such as deafness, partial paralysis from a stroke, and general mental confusion. It is not expected that these patients will be suited to examination in a computer-assisted facility without provisions such as special training. The preliminary initial results show that with the equipment now, 83% of the patients could get a satisfactory distance prescription. With further development, it is expected that as many as 96% of the patients will be able to benefit from such a facility. It is our goal over the next fiscal year to raise these percentages from the former to the latter.

FACILITIES TO BE USED: Optometry Clinic LAMC

FUND: Funded by USA Medical Research and Development Command contract with the University of California Berkeley.

PUBLICATION & CONCLUSIONS: None.

WORK UNIT NO. 431

TITLE OF PROJECT: Enteropathogenic E. Coli-Infant-Adult Transmission studies and Tests of Enteropathogenicity in the Mouse and Guinea Pig Tests

INVESTIGATORS: Principal: Fred R. Stark, LTC, MC

Associate: None

OBJECTIVE: Study in detail the nature of the modes of transmission, and methods of control, and require laboratory confirmation that the 500 strains of E. Coli isolated from infants and volunteers are in fact enteropathogenic by any of three mechanisms presently recognezed.

TECHNICAL APPROACH: Project completed.

Military health care personnel exposed to large numbers of children from a Third World Country with diarrheal disease were shown in this study to be at considerable risk (30-45% attack rates) of contacting acute diarrheal disease despite adequate gowning and handwashing facilities. The principal agents transmitted under "medically favorable" circumstances were shown to be a series of serologically heterogenous enterotoxigenic E. coli, principally providing heat stable toxin, routine in the mouse intestinal system. Strong evidence of airborne transmission was adduced by an extensive epidemiological survey of food handlers, pharmacists and military police with no physical exposure to the children or their families.

A strict "hospital" model of care, where larger space per infant (5.8 sq/m./child vs. 2 sq/m./child) and isolation of individuals with explosive diarrhea appeared to be the principal factors lessening transmission.

It is proposed that if infants from Third World Countries are to be cared for in groups in the United States or other developed countries the standards of the American Academy of Pediatrics for newborn infants be adhered to strictly. In an emergency situation, this suggests decentralization and the utilization of motels and hotels with better space and handwashing/bathing facilities.

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